

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)  
reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)  
reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe  
5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

5 The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1\_1, EZRI\_BOVIN, GGU19889\_1, CC3\_YEAST, S74244, NALS\_MOUSE, MOES\_PIG, S28660, S44860 and YNA4\_CAEEL.

#### EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

20 DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

25 The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH\_1, GIBMUC1A\_1, P\_R96298, AF001406\_1, PVU88874\_1, P\_R85151, AF041409\_1, CELC50F2\_7, C45875, and AB009510\_21.

35 Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

**EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYP0\_HUMAN, AF049498\_1, GEN14531, P\_W14146, HS46KDA\_1, CINB\_RAT, OX2G\_RAT, D87018\_1, and D86996\_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

**EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

in Example 1 above. This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

- 5     forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395).  
      reverse PCR primer 5'-CAGGGACACACTCTACCATTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

- hybridization probe  
10     5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

- 15     DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

- The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

- 25     An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305,  
30     GEN13490, I53641, S53363, HA34\_BRELC, SP96\_DICDI, S36326, SSU51197\_10, MUC1\_XENLA, TCU32448\_1 and AF000409\_1.

#### EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

- 35     Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing



homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

5 In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

10 The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned  
15 ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff  
20 sequences: MGNENDOBX\_1, CELF41G3\_9, AMPG\_STRLI, HSBBOVHERL\_2, LEEXTEN10\_1, AF029958\_1 and P\_W04957.

#### EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70  
30 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST  
35 sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1\_YEAST, AF041382\_1, MAOM\_SOLTU, SPPBPHU9\_1, I41024, EPCPLCFail\_1, HSPLEC\_1, YKL4\_CAEEL, A44643, TGU65922\_1.

#### EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAACTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

hybridization probe

5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure 288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of

the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298\_1, TETN\_CARSP, TETN\_HUMAN, MABA\_RAT, S34198, P\_W13144, MACMBPA\_1, A46274, PSPD\_RAT AND P\_R32188.

10 EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

20 In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

25 The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of approximately 8.76.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA\_THETH, GEN11167, MTV044\_4, AB011151\_1, RLAJ2750\_3, SNEIPTRA\_1, S63624, C28391, A37907, and S14064.

35 Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

**EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P\_W07607, AB000545\_1, AB000546\_1, A1AT\_RAT, AB015164\_1, P\_P50021, COTR\_CAVPO, and HAMHPP\_1. The variants claimed in this application exclude these sequences.

**EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

5 The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned  
10 ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486\_1, AF044205\_1, P\_W31186, CELK03C7\_1, F69034, EF1A\_METVA, AF024540\_1, SSU90353\_1,  
15 MRSP\_STAAU and P\_R97680.

#### EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety  
20 of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a  
25 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.  
30 The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71.  
35 Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about

amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699\_1, S49589, FIBA\_PARPA, FIBB\_HUMAN, P\_R47189, AF004326\_1, DRTENASCN\_1, AF004327\_1, P\_W01411 and FIBG\_BOVIN.

EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1\_YEAST, BPU43599\_1, YS8A\_CAEEL, S67570, LSU54556\_2, S70305, VGLX\_HSVB, and D88733\_1.

**EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375**

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198\_5, CELR12C12\_5, S73465, Y011\_MYCPN, S64538\_1, P\_P8150, MUVSHPO10\_1, VSH\_MUMPL and CVU59751\_5.

**EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385**

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8\_1, LMNACHRA1\_1, HXD9\_HUMAN, CHKCMLF\_1, HS5PP34\_2, DMDRING\_1, A37107\_1, MMLUNGENE\_1, PUM\_DROME and DMU25117\_1.

#### EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence



of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid 379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P\_W36955, MYP0\_HETFR, HS46KDA\_1, AF049498\_1, MYO0\_HUMAN, AF030454\_1, A53268, SHPTCRA\_1, P\_W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGCAGCCCCTGTGACACAACTGG-3' (SEQ ID NO:425)

reverse PCR primer 5'-CTGAGATAACCGAGCCATCTCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II

transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819\_1, HSAJ1687\_1, AF009511\_1, AB010710\_1, GEN13595, HSAJ673\_1, GEN13961, AB005900\_1, LECH\_CHICK, AF021349\_1, and NK13\_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

**EXAMPLE 139: Use of PRO as a hybridization probe**

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

**EXAMPLE 140: Expression of PRO in *E. coli***

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., *Gene*, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., *supra*. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate•2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO<sub>4</sub>) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

*E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column

using a mobile buffer of 0.1 % TFA with elution with a gradient of acetonitrile from 10 to 80 %. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10  $\mu$ g pRK5-PRO DNA is mixed with about 1  $\mu$ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500  $\mu$ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M  $\text{CaCl}_2$ . To this mixture is added, dropwise, 500  $\mu$ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM  $\text{NaPO}_4$ , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200  $\mu$ Ci/ml  $^{35}\text{S}$ -cysteine and 200  $\mu$ Ci/ml  $^{35}\text{S}$ -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to

maximal density in a spinner flask and 700 µg pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 µg/ml bovine insulin and 0.1 µg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO<sub>4</sub> or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as <sup>35</sup>S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni<sup>2+</sup>-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect<sup>®</sup> (Quiagen), Dosper<sup>®</sup> or Eugene<sup>®</sup> (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10<sup>-7</sup> cells are frozen

in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2  $\mu$ m filtered PS20 with 5% 0.2  $\mu$ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with  $3 \times 10^5$  cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at  $1.2 \times 10^6$  cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22  $\mu$ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275  $\mu$ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding

PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni<sup>2+</sup>-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound

protein. After reaching  $A_{280}$  baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with  $Ni^{2+}$ -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

#### EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

#### EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the



art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 146: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is

separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

#### EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced

peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

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EXAMPLE 148: Stimulation of Heart Neonatal Hypertrophy (Assay 1)

This assay is designed to measure the ability of PRO polypeptides to stimulate hypertrophy of neonatal heart. PRO polypeptides testing positive in this assay are expected to be useful for the therapeutic treatment of various cardiac insufficiency disorders.

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Cardiac myocytes from 1-day old Harlan Sprague Dawley rats were obtained. Cells (180  $\mu$ l at  $7.5 \times 10^4$ /ml, serum <0.1%, freshly isolated) are added on day 1 to 96-well plates previously coated with DMEM/F12 + 4% FCS. Test samples containing the test PRO polypeptide or growth medium only (negative control) (20  $\mu$ l/well) are added directly to the wells on day 1. PGF (20  $\mu$ l/well) is then added on day 2 at final concentration of  $10^{-6}$  M. The cells are then stained on day 4 and visually scored on day 5, wherein cells showing no increase in size as compared to negative controls are scored 0.0, cells showing a small to moderate increase in size as compared to negative controls are scored 1.0 and cells showing a large increase in size as compared to negative controls are scored 2.0. A positive result in the assay is a score of 1.0 or greater.

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The following polypeptides tested positive in this assay: PRO1312.

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EXAMPLE 149: Stimulation of Endothelial Cell Proliferation (Assay 8)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

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Bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus VEGF (5 ng/ml); and (4) ACE cells plus FGF (5ng/ml). The control or test sample, (in 100 microliter volumes), was then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO<sub>2</sub>. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of a PRO polypeptide was calculated as the fold increase in proliferation (as determined by the acid phosphatase activity, OD 405 nm) relative to (1) cell only background, and (2) relative to maximum stimulation by VEGF. VEGF (at 3-10 ng/ml) and FGF (at 1-5 ng/ml) were employed as an activity reference for maximum stimulation. Results of the assay were considered "positive" if the observed stimulation was  $\geq$  50% increase over background. VEGF (5 ng/ml) control at 1% dilution gave 1.24 fold stimulation; FGF (5 ng/ml) control at 1% dilution gave 1.46 fold stimulation.

The following PRO polypeptides tested positive in this assay: PRO1154 and PRO1186.

EXAMPLE 150: Inhibition of Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)

The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Polypeptides testing positive in this assay are useful for inhibiting endothelial cell growth in mammals where such an effect would be beneficial, e.g., for inhibiting tumor growth.

Specifically, bovine adrenal cortical capillary endothelial cells (ACE) (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus 5 ng/ml FGF; (4) ACE cells plus 3 ng/ml VEGF; (5) ACE cells plus 3 ng/ml VEGF plus 1 ng/ml TGF-beta; and (6) ACE cells plus 3 ng/ml VEGF plus 5 ng/ml LIF. The test samples, poly-his tagged PRO polypeptides (in 100 microliter volumes), were then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO<sub>2</sub>. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of PRO polypeptides was calculated as the percent inhibition of VEGF (3 ng/ml) stimulated proliferation (as determined by measuring acid phosphatase activity at OD 405 nm) relative to the cells without stimulation. TGF-beta was employed as an activity reference at 1 ng/ml, since TGF-beta blocks 70-90% of VEGF-stimulated ACE cell proliferation. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis. Numerical values (relative inhibition) are determined by calculating the percent inhibition of VEGF stimulated proliferation by the PRO polypeptides relative to cells without stimulation and then dividing that percentage into the percent inhibition obtained by TGF- $\beta$  at 1 ng/ml which is known to block 70-90% of VEGF stimulated cell proliferation. The results are considered positive if the PRO polypeptide exhibits 30% or greater inhibition of VEGF stimulation of endothelial cell growth (relative inhibition 30% or greater).

The following polypeptide tested positive in this assay: PRO812.

**EXAMPLE 151: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)**

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50 :1 of irradiated stimulator cells, and

50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10<sup>7</sup> cells/ml of assay media. The assay is then conducted as described above.

Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO826, PRO1068, PRO1184, PRO1346 and PRO1375.

**EXAMPLE 152: Retinal Neuron Survival (Assay 52)**

This example demonstrates that certain PRO polypeptides have efficacy in enhancing the survival of retinal neuron cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosa, AMD, etc.

Sprague Dawley rat pups at postnatal day 7 (mixed population: glia and retinal neuronal types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N2 and with or without the specific test PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are stained with calcein AM then fixed using 4% paraformaldehyde and stained with DAPI for determination of total cell count. The total cells (fluorescent) are quantified at 20X objective magnification using CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The effect of various concentration of PRO polypeptides are reported herein where percent survival is calculated by dividing the total number of calcein AM positive cells at 2-3 days in culture by the total number of DAPI-labeled cells at 2-3 days in culture. Anything above 30% survival is considered positive.

The following PRO polypeptides tested positive in this assay using polypeptide concentrations within the range of 0.01% to 1.0% in the assay: PRO828, PRO826, PRO1068 and PRO1132.

#### EXAMPLE 153: Rod Photoreceptor Cell Survival (Assay 56)

This assay shows that certain polypeptides of the invention act to enhance the survival/proliferation of rod photoreceptor cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosa, AMD, etc.

Sprague Dawley rat pups at 7 day postnatal (mixed population: glia and retinal neuronal cell types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N<sub>2</sub>. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are fixed using 4% paraformaldehyde, and then stained using CellTracker Green CMFDA. Rho 4D2 (ascites or IgG 1:100), a monoclonal antibody directed towards the visual pigment rhodopsin is used to detect rod photoreceptor cells by indirect immunofluorescence. The results are calculated as % survival: total number of calcein- rhodopsin positive cells at 2-3 days in culture, divided by the total number of rhodopsin positive cells at time 2-3 days in culture. The total cells (fluorescent) are quantified at 20x objective magnification using a CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The following polypeptides tested positive in this assay: PRO536, PRO943, PRO828, PRO826, PRO1068 and PRO1132.

EXAMPLE 154: Induction of c-fos in Endothelial Cells (Assay 34)

This assay is designed to determine whether PRO polypeptides show the ability to induce c-fos in endothelial cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50% Ham's F12 w/o GHT: low glucose, and 50% DMEM without glycine: with NaHCO<sub>3</sub>, 1% glutamine, 10 mM HEPES, 10% FBS, 10 ng/ml bFGF) were plated on 96-well microtiter plates at a cell density of  $1 \times 10^4$  cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100  $\mu$ l/well test samples and controls (positive control = growth media; negative control = Protein 32 buffer = 10 mM HEPES, 140 mM NaCl, 4% (w/v) mannitol, pH 6.8). The cells were incubated for 30 minutes at 37°C, in 5% CO<sub>2</sub>. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed, where each capitalized reagent/buffer listed below was available from the kit.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100  $\mu$ l of Capture Hybridization Buffer was added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100  $\mu$ l of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortexed on the #2 setting for one minute. 80  $\mu$ l of the lysate was removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the plates were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/ $\mu$ l) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50  $\mu$ l of Amplifier Working Solution was added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/ $\mu$ l) in AL Hybridization Buffer. After the 10-minute cool-down period, the amplifier hybridization mixture was removed and the plates were washed twice with Wash A. 50  $\mu$ l of Label Probe Working Solution was added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room

temperature. Upon addition of 3  $\mu$ l of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three times with Wash D. 50  $\mu$ l of the Substrate Solution with Enhancer was added to each well. The plates were incubated for 30 minutes at 37°C and RLU was read in an appropriate luminometer.

5           The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the negative control (Protein 32/HEPES buffer described above) value was indicated by chemiluminescence units (RLU). The results are considered positive if the PRO polypeptide exhibits at least a two-fold value over the negative buffer control. Negative control = 1.00 RLU at 1.00% dilution. Positive control = 8.39 RLU at 1.00% dilution.

10           The following PRO polypeptides tested positive in this assay: PRO535, PRO826, PRO819, PRO1126, PRO1160 and PRO1387.

EXAMPLE 155: Inhibitory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 67)

15           This example shows that one or more of the polypeptides of the invention are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

          The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

20           More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO<sub>2</sub>) and then washed and resuspended to 3x10<sup>6</sup> cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The  
25           stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

          The assay is prepared by plating in triplicate wells a mixture of:

          100:1 of test sample diluted to 1% or to 0.1%,

          50 :1 of irradiated stimulator cells, and

30           50 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO<sub>2</sub> for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

          In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice.  
35           The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000



rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to  $1 \times 10^7$  cells/ml of assay media. The assay is then conducted as described above.

Any decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein.

5           The following polypeptide tested positive in this assay: PRO1114, PRO836, PRO1159, PRO1312, PRO1192, PRO1195 and PRO1387.

EXAMPLE 156: Mouse Kidney Mesangial Cell Proliferation Assay (Assay 92)

10           This assay shows that certain polypeptides of the invention act to induce proliferation of mammalian kidney mesangial cells and, therefore, are useful for treating kidney disorders associated with decreased mesangial cell function such as Berger disease or other nephropathies associated with Schönlein-Henoch purpura, celiac disease, dermatitis herpetiformis or Crohn disease. The assay is performed as follows. On day one, mouse kidney mesangial cells are plated on a 96 well plate in growth media (3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95% fetal bovine serum, 5% supplemented with 14 mM HEPES) and grown overnight. On day 2, PRO polypeptides are diluted at 2 concentrations (1% and 0.1%) in serum-free medium and added to the cells. Control samples are serum-free medium alone. On day 4, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Progenia) was added to each well and the colorimetric reaction was allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is anything that gives an absorbance reading which is at least 15% above the control reading.

20           The following polypeptide tested positive in this assay: PRO819, PRO813 and PRO1066.

EXAMPLE 157: Pericyte c-Fos Induction (Assay 93)

25           This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100  $\mu$ l of PRO polypeptide test samples and controls. (positive control = DME+5% serum +/- PDGF at 500 ng/ml; negative control = protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading verses frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media = low glucose DMEM = 20% FBS + 1X pen strep + 1X fungizone.

35           Assay Media = low glucose DMEM + 5% FBS.

          The following polypeptides tested positive in this assay: PRO943 and PRO819.

**EXAMPLE 158: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)**

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1114, PRO1007, PRO1066, PRO848, PRO1182, PRO1198, PRO1192, PRO1271, PRO1375 and PRO1387.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1184, PRO1360, PRO1309, PRO1154, PRO1181, PRO1186, PRO1160 and PRO1384.

**EXAMPLE 159: Chondrocyte Re-differentiation Assay (Assay 110)**

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100µl of the same media without serum and 100 µl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 µl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1282, PRO1310, PRO619, PRO943, PRO820, PRO1080, PRO1016, PRO1007, PRO1056, PRO791, PRO1111, PRO1184, PRO1360, PRO1309, PRO1107, PRO1132, PRO1131, PRO848, PRO1181, PRO1186, PRO1159, PRO1312, PRO1192 and PRO1384.

EXAMPLE 160: Chondrocyte Proliferation Assay (Assay 111)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

5 Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm<sup>2</sup> in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm<sup>2</sup> every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of either serum-free medium (negative control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 µl/well. After 5 days at 37°C, 20 µl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 µl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide treated sample is more like that of the positive control than the negative control.

15 The following PRO polypeptides tested positive in this assay: PRO1310, PRO844, PRO1312, PRO1192 and PRO1387.

EXAMPLE 161: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

20 This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is a transcription factor called Pdx1.

25 The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20 µg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

35 14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 µg/ml

Aprotinin (50µg/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60µg/ml

5 Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100µg (BRL 100004)

Triiodothyronine, 10µl of  $5 \times 10^{-6}$  M (Sigma T5516)

10 Ethanolamine, 100µl of  $10^{-1}$  M (Sigma E0135)

Phosphoethalamine, 100µl of  $10^{-1}$  M (Sigma P0503)

Selenium, 4µl of  $10^{-1}$  M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2µl of  $5 \times 10^{-3}$  M (Sigma #H0135)

15 Progesterone, 100µl of  $1 \times 10^{-3}$  M (Sigma #P6149)

Forskolin, 500µl of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10 µg/ml), insulin (1 µg/ml), gentamycin (100 ng/ml), aprotinin (50 µg/ml) and BPE (15 µg/ml).

20 Defined media:

RPMI 1640 plus transferrin (10 µg/ml), insulin (1 µg/ml), gentamycin (100 ng/ml) and aprotinin (50 µg/ml).

The following polypeptides tested positive in this assay: PRO1310, PRO1188, PRO1131 and PRO1387.

25

**EXAMPLE 162: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)**

30 This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

35 In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay

if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO358, PRO1016, PRO1007, PRO826, PRO1066, PRO1029 and PRO1309.

**EXAMPLE 163: Fetal Hemoglobin Induction in an Erythroblastic Cell Line (Assay 107)**

This assay is useful for screening PRO polypeptides for the ability to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line. Molecules testing positive in this assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. The assay is performed as follows. Erythroblastic cells are plated in standard growth medium at 1000 cells/well in a 96 well format. PRO polypeptides are added to the growth medium at a concentration of 0.2% or 2% and the cells are incubated for 5 days at 37°C. As a positive control, cells are treated with 100μM hemin and as a negative control, the cells are untreated. After 5 days, cell lysates are prepared and analyzed for the expression of gamma globin (a fetal marker). A positive in the assay is a gamma globin level at least 2-fold above the negative control.

The following polypeptides tested positive in this assay: PRO1114, PRO826, PRO1066, PRO844, PRO1192 and PRO1358.

**EXAMPLE 164: Induction of Pancreatic β-Cell Precursor Differentiation (Assay 89)**

This assay shows that certain polypeptides of the invention act to induce differentiation of pancreatic β-cell precursor cells into mature pancreatic β-cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is insulin.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20μg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 μg/ml

Aprotinin (50 $\mu$ g/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 $\mu$ g/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

5 Epidermal Growth Factor, 100 $\mu$ g (BRL 100004)

Triiodothyronine, 10 $\mu$ l of 5x10<sup>-6</sup> M (Sigma T5516)

Ethanolamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma E0135)

Phosphoethalamine, 100 $\mu$ l of 10<sup>-1</sup> M (Sigma P0503)

Selenium, 4 $\mu$ l of 10<sup>-1</sup> M (Aesar #12574)

10 Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 $\mu$ l of 5X10<sup>-3</sup> M (Sigma #H0135)

Progesterone, 100 $\mu$ l of 1X10<sup>-3</sup> M (Sigma #P6149)

Forskolin, 500 $\mu$ l of 20mM (Calbiochem #344270)

Minimal media:

15 RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml), aprotinin (50  $\mu$ g/ml) and BPE (15  $\mu$ g/ml).

Defined media:

RPMI 1640 plus transferrin (10  $\mu$ g/ml), insulin (1  $\mu$ g/ml), gentamycin (100 ng/ml) and aprotinin (50  $\mu$ g/ml).

20 The following polypeptides were positive in this assay: PRO1188, PRO1132, PRO1131 and PRO1181.

#### EXAMPLE 165: Skin Vascular Permeability Assay (Assay 64)

25 This assay shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Compounds which stimulate an immune response are useful therapeutically where stimulation of an immune response is beneficial. This skin vascular permeability assay is conducted as follows. Hairless guinea pigs weighing 350 grams or more are anesthetized with ketamine (75-80 mg/Kg) and 5 mg/Kg xylazine intramuscularly (IM). A sample of purified polypeptide of the invention or a conditioned media test sample

30 is injected intradermally onto the backs of the test animals with 100  $\mu$ l per injection site. It is possible to have about 10-30, preferably about 16-24, injection sites per animal. One  $\mu$ l of Evans blue dye (1% in physiologic buffered saline) is injected intracardially. Blemishes at the injection sites are then measured (mm diameter) at 1 hr and 6 hr post injection. Animals were sacrificed at 6 hrs after injection. Each skin injection site is biopsied and fixed in formalin. The skins are then prepared for histopathologic evaluation. Each site is

35 evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least a minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is

scored as negative.

The following polypeptide tested positive in this assay: PRO1007, PRO1358 and PRO1375.

EXAMPLE 166: Induction of Endothelial Cell Apoptosis (ELISA) (Assay 109)

The ability of PRO polypeptides to induce apoptosis in endothelial cells was tested in human venous umbilical vein endothelial cells (HUVEC, Cell Systems) using a 96-well format, in 0% serum media supplemented with 100 ng/ml VEGF, 0.1 % BSA, 1X penn/strep. A positive result in this assay indicates the usefulness of the polypeptide for therapeutically treating any of a variety of conditions associated with undesired endothelial cell growth including, for example, the inhibition of tumor growth. The 96-well plates used were manufactured by Falcon (No. 3072). Coating of 96 well plates were prepared by allowing gelatinization to occur for >30 minutes with 100  $\mu$ l of 0.2% gelatin in PBS solution. The gelatin mix was aspirated thoroughly before plating HUVEC cells at a final concentration of  $2 \times 10^4$  cells/ml in 10% serum containing medium - 100  $\mu$ l volume per well. The cells were grown for 24 hours before adding test samples containing the PRO polypeptide of interest.

To all wells, 100  $\mu$ l of 0% serum media (Cell Systems) complemented with 100 ng/ml VEGF, 0.1% BSA, 1X penn/strep was added. Test samples containing PRO polypeptides were added in triplicate at dilutions of 1%, 0.33% and 0.11%. Wells without cells were used as a blank and wells with cells only were used as a negative control. As a positive control, 1:3 serial dilutions of 50  $\mu$ l of a 3x stock of staurosporine were used. The cells were incubated for 24 to 35 hours prior to ELISA.

ELISA was used to determine levels of apoptosis preparing solutions according to the Boehringer Manual [Boehringer, Cell Death Detection ELISA plus, Cat No. 1 920 685]. Sample preparations: 96 well plates were spun down at 1 krpm for 10 minutes (200g); the supernatant was removed by fast inversion, placing the plate upside down on a paper towel to remove residual liquid. To each well, 200  $\mu$ l of 1X Lysis buffer was added and incubation allowed at room temperature for 30 minutes without shaking. The plates were spun down for 10 minutes at 1 krpm, and 20  $\mu$ l of the lysate (cytoplasmic fraction) was transferred into streptavidin coated MTP. 80  $\mu$ l of immunoreagent mix was added to the 20  $\mu$ l lysate in each well. The MTP was covered with adhesive foil and incubated at room temperature for 2 hours by placing it on an orbital shaker (200 rpm). After two hours, the supernatant was removed by suction and the wells rinsed three times with 250  $\mu$ l of 1X incubation buffer per well (removed by suction). Substrate solution was added (100  $\mu$ l) into each well and incubated on an orbital shaker at room temperature at 250 rpm until color development was sufficient for a photometric analysis (approx. after 10-20 minutes). A 96 well reader was used to read the plates at 405 nm, reference wavelength, 492 nm. The levels obtained for PIN 32 (control buffer) was set to 100%. Samples with levels > 130% were considered positive for induction of apoptosis.

The following PRO polypeptides tested positive in this assay: PRO844.

EXAMPLE 167: Guinea Pig Vascular Leak (Assay 32)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce vascular permeability. Polypeptides testing positive in this assay are expected to be useful

for the therapeutic treatment of conditions which would benefit from enhanced vascular permeability including, for example, conditions which may benefit from enhanced local immune system cell infiltration.

Hairless guinea pigs weighing 350 grams or more were anesthetized with Ketamine (75-80 mg/kg) and 5 mg/kg Xylazine intramuscularly. Test samples containing the PRO polypeptide or a physiological buffer without the test polypeptide are injected into skin on the back of the test animals with 100  $\mu$ l per injection site intradermally. There were approximately 16-24 injection sites per animal. One ml of Evans blue dye (1% in PBS) is then injected intracardially. Skin vascular permeability responses to the compounds (*i.e.*, blemishes at the injection sites of injection) are visually scored by measuring the diameter (in mm) of blue-colored leaks from the site of injection at 1, 6 and 24 hours post administration of the test materials. The mm diameter of blueness at the site of injection is observed and recorded as well as the severity of the vascular leakage. Blemishes of at least 5 mm in diameter are considered positive for the assay when testing purified proteins, being indicative of the ability to induce vascular leakage or permeability. A response greater than 7 mm diameter is considered positive for conditioned media samples. Human VEGF at 0.1  $\mu$ g/100  $\mu$ l is used as a positive control, inducing a response of 4-8 mm diameter.

The following PRO polypeptides tested positive in this assay: PRO1155.

**EXAMPLE 168: Mouse Mesengial Cell Inhibition Assay (Assay 114)**

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to inhibit the proliferation of mouse mesengial cells in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of such diseases or conditions where inhibition of mesengial cell proliferation would be beneficial such as, for example, cystic renal dysplasia, polycystic kidney disease, or other kidney disease assoicated with abnormal mesengial cell proliferation, renal tumors, and the like.

On day 1, mouse mesengial cells are plated on a 96 well plate in growth medium (a 3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95%; fetal bovine serum, 5%; supplemented with 14mM HEPES) and then are allowed to grow overnight. On day 2, the PRO polypeptide is diluted at 2 different concentrations (1%, 0.1%) in serum-free medium and is added to the cells. The negative control is growth medium without added PRO polypeptide. After the cells are allowed to incubate for 48 hours, 20  $\mu$ l of the Cell Titer 96 Aqueous one solution reagent (Promega) is added to each well and the colormetric reaction is allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay is an absorbance reading which is at least 10% above the negative control.

The following PRO polypeptides tested positive in this assay: PRO1192 and PRO1195.

**Example 169: *In Vitro* Antitumor Assay (Assay 161)**

The antiproliferative activity of various PRO polypeptides was determined in the investigational, disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., J. Natl. Cancer Inst. 82:1107-1112 (1990). The 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions



for their maintenance and culture *in vitro* have been described by Monks et al., J. Natl. Cancer Inst. 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, Cancer: Princ. Pract. Oncol. Update 3(10):1-12 [1989]).

5 Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco), washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100  $\mu$ L volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero in 100  $\mu$ L aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log  
10 dilutions (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO<sub>2</sub> atmosphere and 100% humidity.

After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid  
15 to remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris base [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The results are shown in the following table, where the abbreviations are as follows:

20 NSCL = non-small cell lung carcinoma

CNS = central nervous system

Table 7

	Test compound	Concentration	Days	Tumor Cell Line Type	C e l l L i n e
					Designation
25	PRO1016	0.1 nM	2	Leukemia	K-568
	PRO1016	0.1 nM	2	Leukemia	MOLT-4
	PRO1016	0.1 nM	2	Leukemia	RPMI-8226
	PRO1016	0.1 nM	2	NSCL	A549/ATCC
30	PRO1016	0.1 nM	2	NSCL	EKVX
	PRO1016	0.1 nM	2	NSCL	NCI-H23
	PRO1016	0.1 nM	2	NSCL	NCI-H522
	PRO1016	0.1 nM	2	Colon	KM-12
35	PRO1016	0.1 nM	2	CNS	SF-295
	PRO1016	0.1 nM	2	Melanoma	SK-MEL-5
	PRO1016	0.1 nM	2	Melanoma	UACC-257
	PRO1016	0.1 nM	2	Ovarian	OVCAR-3
40	PRO1016	0.1 nM	2	Ovarian	OVCAR-4
	PRO1016	0.1 nM	2	Breast	NCI/SDR-RES
	PRO1016	0.1 nM	2	Breast	T-47D
	PRO1016	0.1 nM	6	Leukemia	CCRF-CEM
	PRO1016	0.1 nM	6	Leukemia	K-562

Table 7 (cont')

	Test compound	Concentration	Days	Tumor Cell Line Type	C e l l L i n e
					Designation
5	PRO1016	0.1 nM	6	Leukemia	MOLT-4
	PRO1016	0.1 nM	6	Leukemia	RPMI-8226
	PRO1016	0.1 nM	6	NSCL	A549/ATCC
	PRO1016	0.1 nM	6	NSCL	EKVX
	PRO1016	0.1 nM	6	NSCL	HOP-62
10	PRO1016	0.1 nM	6	NSCL	NCI-H23
	PRO1016	0.1 nM	6	NSCL	NCI-H322M
	PRO1016	0.1 nM	6	NSCL	NCI-H460
	PRO1016	0.1 nM	6	NSCL	NCI-H522
	PRO1016	0.1 nM	6	Colon	COLO 205
15	PRO1016	0.1 nM	6	Colon	CHT-116
	PRO1016	0.1 nM	6	Colon	HCT-15
	PRO1016	0.1 nM	6	Colon	HT-29
	PRO1016	0.1 nM	6	Colon	SW-620
	PRO1016	0.1 nM	6	CNS	SF-295
20	PRO1016	0.1 nM	6	CNS	SF-539
	PRO1016	0.1 nM	6	CNS	SNB-19
	PRO1016	0.1 nM	6	CNS	U251
	PRO1016	0.1 nM	6	Melanoma	LOX IMVI
	PRO1016	0.1 nM	6	Melanoma	MALME-3M
25	PRO1016	0.1 nM	6	Melanoma	SK-MEL-28
	PRO1016	0.1 nM	6	Melanoma	SK-MEL-5
	PRO1016	0.1 nM	6	Melanoma	UACC-257
	PRO1016	0.1 nM	6	Melanoma	UACC-62
	PRO1016	0.1 nM	6	Ovarian	IGROV1
30	PRO1016	0.1 nM	6	Ovarian	OVCAR-3
	PRO1016	0.1 nM	6	Ovarian	OVCAR-4
	PRO1016	0.1 nM	6	Ovarian	OVCAR-8
	PRO1016	0.1 nM	6	Renal	ACHN
	PRO1016	0.1 nM	6	Renal	RXF 393
35	PRO1016	0.1 nM	6	Renal	SN12C
	PRO1016	0.1 nM	6	Renal	TK-10
	PRO1016	0.1 nM	6	Prostate	PC-3
	PRO1016	0.1 nM	6	Breast	MCF-7
	PRO1016	0.1 nM	6	Breast	NCI/ADR-RES
40	PRO1016	0.1 nM	6	Breast	MDA-MB-231
	PRO1016	0.1 nM	6	Breast	MDA-MB-435
	PRO1016	0.1 nM	6	Breast	MDA-N
	PRO1016	0.1 nM	6	Breast	BT-549
	PRO1016	0.1 nM	6	Breast	T-47D
45	PRO1186	95 nM	2	NSCL	NCI-H226
	PRO1186	95 nM	2	Colon	Colo205
	PRO1186	2.2 nM	6	Breast	MDA-N
	PRO1186	114 nM	2	NSCL	NCI-H322M
	PRO1186	114 nM	2	CNS	SF-268; SF-539
50	PRO1186	114 nM	2	Ovarian	IGFOV1
	PRO1186	114 nM	2	Renal	786-0; SN12C; TK-10
	PRO1186	114 nM	6	Leukemia	MOLT-4; RPMI-8226
	PRO1186	114 nM	6	Melanoma	LOX IMVI
	PRO1186	114 nM	6	Ovarian	OVCAR-4; SK-OV-3

Table 7 (cont')

	Test compound	Concentration	Days	Tumor Cell Line Type	Cell Line
					Designation
	PRO1186	114 nM	6	Breast	MDA-MB-435; T-47D
5	PRO1186	8.1 nM	6	Leukemia	K-562
	PRO1186	8.1 nM	6	NSCL	HOP-62
	PRO1186	8.1 nM	6	Colon	Colo205; HCC-2998
	PRO1186	8.1 nM	6	Breast	T-47D
	PRO1186	15.4 nM	6	Leukemia	K-562
10	PRO1186	3.6 nM	2	Ovarian	OVCAR-3
	PRO1186	3.6 nM	6	NSCL	HOP-62

The results of these assays demonstrate that the positive testing PRO polypeptides are useful for inhibiting neoplastic growth in a number of different tumor cell types and may be used therapeutically therefor.. Antibodies against these PRO polypeptides are useful for affinity purification of these useful polypeptides. Nucleic acids encoding these PRO polypeptides are useful for the recombinant preparation of these polypeptides.

#### EXAMPLE 170: Gene Amplification in Tumors

This example shows that certain PRO polypeptide-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers and diagnostic determination of the presence of those cancers. Therapeutic agents may take the form of antagonists of the PRO polypeptide, for example, murine-human chimeric, humanized or human antibodies against a PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8. An explanation of the abbreviations used for the designation of the primary tumors listed in Table 8 and the primary tumors and cell lines referred to throughout this example are given below.

The results of the TaqMan™ are reported in delta ( $\Delta$ ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TaqMan™ fluorescent probe derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide-encoding gene which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are

preferred for the primer and probe derivation, *e.g.*, 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO polypeptide gene amplification analysis were as follows:

PRO290 (DNA35680-1212):

35680.tm.p:

5 5'-CCACCAATGGCAGCCCCACCT-3' (SEQ ID NO:428)

35680.tm.f:

5'-GACTGCCCTCCCTGCCA-3' (SEQ ID NO:429)

35680.tm.r:

10 5'-CAAAAAGCCTGGAAGCTTCAAAG-3' (SEQ ID NO:430)

PRO341 (DNA26288-1239):

26288.tm.fl:

5'-CAGCTGGACTGCAGGTGCTA-3' (SEQ ID NO:431)

26288.tm.rl:

15 5'-CAGTGAGCACAGCAAGTGCCT-3' (SEQ ID NO:432)

26288.tm.pl:

5'-GGCCACCTCCTTGAGTCTTCAGTTCCT-3' (SEQ ID NO:433)

PRO535 (DNA49143-1429):

20 49143.tm.fl:

5'-CAACTACTGGCTAAAGCTGGTGAA-3' (SEQ ID NO:434)

49143.tm.rl:

5'-CCTTTCTGTATAGGTGATACCCAATGA-3' (SEQ ID NO:435)

49143.tm.pl:

25 5'-TGGCCATCCCTACCAGAGGCAAAA-3' (SEQ ID NO:436)

PRO619 (DNA49821-1562):

49821.tm.fl:

5'-CTGAAGACGACGCGGATTACTA-3' (SEQ ID NO:437)

30 49821.tm.rl:

5'-GGCAGAAATGGGAGGCAGA-3' (SEQ ID NO:438)

49821.tm.pl:

5'-TGCTCTGTTGGCTACGGCTTAGTCCCTAG-3' (SEQ ID NO:439)

35 PRO809 (DNA57836-1338):

57836.tm.fl:

5'-AGCAGCAGCCATGTAGAATGAA-3' (SEQ ID NO:440)

57836.tm.rl:

5'-AATACGAACAGTGCACGCTGAT-3' (SEQ ID NO:441)

57836.tm.pl:

5'-TCCAGAGAGCCAAGCACGGCAGA-3' (SEQ ID NO:442)

5 PRO830 (DNA56866-1342):56866.tm.fl:

5'-TCTAGCCAGCTTGGCTCCAATA-3' (SEQ ID NO:443)

56866.tm.rl:

5'-CCTGGCTCTAGCACCAACTCATA-3' (SEQ ID NO:444)

10 56866.tm.pl:

5'-TCAGTGGCCCTAAGGAGATGGGCCT-3' (SEQ ID NO:445)

PRO848 (DNA59839-1461):59839.tm.fl:

15 5'-CAGGATACAGTGGGAATCTTGAGA-3' (SEQ ID NO:446)

59839.tm.rl:

5'-CCTGAAGGGCTTGGAGCTTAGT-3' (SEQ ID NO:447)

59839.tm.pl:

5'-TCTTTGGCCATTTCCTATGGCTCA-3' (SEQ ID NO:448)

20

PRO943 (DNA52192-1369):52192.tm.fl:

5'-CCCATGGCGAGGAGGAAT-3' (SEQ ID NO:449)

52192.tm.rl:

25 5'-TGCGTACGTGTGCCTTCAG-3' (SEQ ID NO:450)

52192.tm.pl:

5'-CAGCACCCCAGGCAGTCTGTGTGT-3' (SEQ ID NO:451)

PRO1005 (DNA57708-1411):30 57708.tm.fl:

5'-AACGTGCTACACGACCAGTGTACT-3' (SEQ ID NO:452)

57708.tm.rl:

5'-CACAGCATATTCAGATGACTAAATCCA-3' (SEQ ID NO:453)

57708.tm.pl:

35 5'-TTGTTTAGTTCTCCACCGTGTCTCCACAGAA-3' (SEQ ID NO:454)

PRO1009 (DNA57129-1413):57129.tm.fl:

5'-TGTCAGAATGCAACCTGGCTT-3' (SEQ ID NO:455)

57129.tm.rl:

5'-TGATGTGCCTGGCTCAGAAC-3' (SEQ ID NO:456)

5 57129.tm.pl:

5'-TGCACCTAGATGTCCCCAGCACCC-3' (SEQ ID NO:457)

PRO1097 (DNA59841-1460):59841.tm.fl:

10 5'-AAGATGCGCCAGGCTTCTTA-3' (SEQ ID NO:458)

59841.tm.rl:

5'-CTCCTGTACGGTCTGCTCACTTAT-3' (SEQ ID NO:459)

59841.tm.pl:

15 5'-TGGCTGTCAGTCCAGTGTGCATGG-3' (SEQ ID NO:460)

PRO1107 (DNA59606-1471):59606.tm.fl:

5'-GCATAGGGATAGATAAGATCCTGCTTTAT-3' (SEQ ID NO:461)

59606.tm.rl:

20 5'-CAAATTAAAGTACCCATCAGGAGAGAA-3' (SEQ ID NO:462)

59606.tm.pl:

5'-AAGTTGCTAAATATATACATTATCTGCGCCAAGTCCA-3' (SEQ ID NO:463)

PRO1111 (DNA58721-1475):25 58721.tm.fl:

5'-GTGCTGCCCACAATTCATGA-3' (SEQ ID NO:464)

58721.tm.rl:

5'-GTCCTTGGTATGGGTCTGAATTATAT-3' (SEQ ID NO:465)

58721.tm.pl:

30 5'-ACTCTCTGCACCCACAGTCACCACTATCTC-3' (SEQ ID NO:466)

PRO1153 (DNA59842-1502):59842.tm.fl:

5'-CTGAGGAACCAGCCATGTCTCT-3' (SEQ ID NO:467)

35 59842.tm.rl:

5'-GACCAGATGCAGGTACAGGATGA-3' (SEQ ID NO:468)

59842.tm.pl:

5'-CTGCCCCCTTCAGTGATGCCAACCTT-3' (SEQ ID NO:469)

PRO1182 (DNA59848-1512):59848.tm.fl:

5 5'-GGGTGGAGGCTCACTGAGTAGA-3' (SEQ ID NO:470)

59848.tm.rl:

5'-CAATACAGGTAATGAACTCTGCTTCTT-3' (SEQ ID NO:471)

59848.tm.pl:

10 5'-TCCTCTTAAGCATAGGCCATTTTCTCAGTTTAGACA-3' (SEQ ID NO:472)

PRO1184 (DNA59220-1514):59220.tm.fl:

5'-GGTGGTCTTGCTTGGTCTCAC-3' (SEQ ID NO:473)

59220.tm.rl:

15 5'-CCGTCGTTTCAGCAACATGAC-3' (SEQ ID NO:474)

59220.tm.pl:

5'-ACCGCCTACCGCTGTGCCCA-3' (SEQ ID NO:475)

PRO1187 (DNA62876-1517):20 62876.tm.fl:

5'-CAGTAAAACACAGGCTGGATTT-3' (SEQ ID NO:476)

62876.tm.rl:

5'-CCTGAGAGCAAGAAGGTTGAGAAT-3' (SEQ ID NO:477)

62876.tm.pl:

25 5'-TAGACAGGGACCATGGCCCGCA-3' (SEQ ID NO:478)

PRO1281 (DNA59820-1549):59820.tm.fl:

5'-TGGGCTGTAGAAGAGTTGTTG-3' (SEQ ID NO:479)

30 59820.tm.rl:

5'-TCCACACTTGGCCAGTTTAT-3' (SEQ ID NO:480)

59820.tm.pl:

5'-CCCAACTTCTCCCTTTTGGACCCT-3' (SEQ ID NO:481)

35 PRO1112 (DNA57702-1476):57702.tm.fl

5'-GTCCCTTCACTGTTTAGAGCATGA-3' (SEQ ID NO:482)

57702.tm.p1

5'-ACTCTCCCCCTCAACAGCCTCCTGAG-3' (SEQ ID NO:483)

57702.tm.r1

5'-GTGGTCAGGGCAGATCCTTT-3' (SEQ ID NO:484)

5 PRO1185 (DNA62881-1515):62881.tm.f1:

5'-ACAGATCCAGGAGAGACTCCACA -3' (SEQ ID NO:485)

62881.tm.p1:

5'-AGCGGCGCTCCCAGCCTGAAT -3' (SEQ ID NO:486)

10 62881.tm.r1:

5'-CATGATTGGTCCTCAGTTCCATC -3' (SEQ ID NO:487)

PRO1245 (DNA64884-1527):64884.tm.f1:

15 5'-ATAGAGGGCTCCCAGAAGTG -3' (SEQ ID NO:488)

64884.tm.p1:

5'-CAGGGCCTTCAGGGCCTTCAC-3' (SEQ ID NO:489)

64884.tm.r1:

5'-GCTCAGCCAAACACTGTCA-3' (SEQ ID NO:490)

20 64884.tm.f2:

5'-GGGGCCCTGACAGTGTT -3' (SEQ ID NO:491)

64884.tm.p2:

5'-CTGAGCCGAGACTGGAGCATCTACAC-3' (SEQ ID NO:492)

64884.tm.r2:

25 5'-GTGGGCAGCGTCTTGTC-3' (SEQ ID NO:493)

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers (forward [.f] and reverse [.r]) are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe (.p), is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.



The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700™ Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The  $\Delta C_t$  values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results.

Table 8 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO polypeptide compounds of the invention.

Table 8  
Primary Lung and Colon Tumor Profiles

	Primary Tumor Stage	Stage	Other Stage	Dukes Stage	T Stage	N Stage
5	Human lung tumor AdenoCa (SRCC724) [LT1]	IIA			T1	N1
	Human lung tumor SqCCa (SRCC725) [LT1a]	IIB			T3	N0
	Human lung tumor AdenoCa (SRCC726) [LT2]	IB			T2	N0
	Human lung tumor AdenoCa (SRCC727) [LT3]	IIIA			T1	N2
	Human lung tumor AdenoCa (SRCC728) [LT4]	IB			T2	N0
10	Human lung tumor SqCCa (SRCC729) [LT6]	IB			T2	N0
	Human lung tumor Aden/SqCCa (SRCC730) [LT7]	IA			T1	N0
	Human lung tumor AdenoCa (SRCC731) [LT9]	IB			T2	N0
	Human lung tumor SqCCa (SRCC732) [LT10]	IIB			T2	N1
	Human lung tumor SqCCa (SRCC733) [LT11]	IIA			T1	N1
15	Human lung tumor AdenoCa (SRCC734) [LT12]	IV			T2	N0
	Human lung tumor AdenoSqCCa (SRCC735)[LT13]	IB			T2	N0
	Human lung tumor SqCCa (SRCC736) [LT15]	IB			T2	N0
	Human lung tumor SqCCa (SRCC737) [LT16]	IB			T2	N0
	Human lung tumor SqCCa (SRCC738) [LT17]	IIB			T2	N1
20	Human lung tumor SqCCa (SRCC739) [LT18]	IB			T2	N0
	Human lung tumor SqCCa (SRCC740) [LT19]	IB			T2	N0
	Human lung tumor LCCa (SRCC741) [LT21]	IIB			T3	N1
	Human lung AdenoCa (SRCC811) [LT22]	IA			T1	N0
	Human colon AdenoCa (SRCC742) [CT2]		M1	D	pT4	N0
25	Human colon AdenoCa (SRCC743) [CT3]			B	pT3	N0
	Human colon AdenoCa (SRCC744) [CT8]			B	T3	N0
	Human colon AdenoCa (SRCC745) [CT10]			A	pT2	N0
	Human colon AdenoCa (SRCC746) [CT12]		MO, R1	B	T3	N0
	Human colon AdenoCa (SRCC747) [CT14]		pMO, RO	B	pT3	pN0
30	Human colon AdenoCa (SRCC748) [CT15]		M1, R2	D	T4	N2
	Human colon AdenoCa (SRCC749) [CT16]		pMO	B	pT3	pN0
	Human colon AdenoCa (SRCC750) [CT17]			C1	pT3	pN1
	Human colon AdenoCa (SRCC751) [CT1]		MO, R1	B	pT3	N0
	Human colon AdenoCa (SRCC752) [CT4]			B	pT3	M0
35	Human colon AdenoCa (SRCC753) [CT5]		G2	C1	pT3	pN0
	Human colon AdenoCa (SRCC754) [CT6]		pMO, RO	B	pT3	pN0
	Human colon AdenoCa (SRCC755) [CT7]		G1	A	pT2	pN0
	Human colon AdenoCa (SRCC756) [CT9]		G3	D	pT4	pN2
	Human colon AdenoCa (SRCC757) [CT11]			B	T3	N0
40	Human colon AdenoCa (SRCC758) [CT18]		MO, RO	B	pT3	pN0

#### DNA Preparation:

DNA was prepared from cultured cell lines, primary tumors, normal human blood. The isolation was performed using purification kit, buffer set and protease and all from Quiagen, according to the manufacturer's instructions and the description below.

#### Cell culture lysis:

Cells were washed and trypsinized at a concentration of  $7.5 \times 10^8$ -per tip and pelleted by centrifuging at 1000 rpm for 5 minutes at 4°C, followed by washing again with 1/2 volume of PBS recentrifugation. The pellets were washed a third time, the suspended cells collected and washed 2x with PBS. The cells were then suspended into 10 ml PBS. Buffer C1 was equilibrated at 4°C. Qiagen protease #19155 was diluted into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and equilibrated at 4°C. 10 ml of G2 Buffer was prepared

by diluting Qiagen RNase A stock (100 mg/ml) to a final concentration of 200  $\mu$ g/ml.

Buffer C1 (10 ml, 4°C) and ddH<sub>2</sub>O (40 ml, 4°C) were then added to the 10 ml of cell suspension, mixed by inverting and incubated on ice for 10 minutes. The cell nuclei were pelleted by centrifuging in a Beckman swinging bucket rotor at 2500 rpm at 4°C for 15 minutes. The supernatant was discarded and the nuclei were suspended with a vortex into 2 ml Buffer C1 (at 4°C) and 6 ml ddH<sub>2</sub>O, followed by a second 4°C centrifugation at 2500 rpm for 15 minutes. The nuclei were then resuspended into the residual buffer using 200  $\mu$ l per tip. G2 buffer (10 ml) was added to the suspended nuclei while gentle vortexing was applied. Upon completion of buffer addition, vigorous vortexing was applied for 30 seconds. Quiagen protease (200  $\mu$ l, prepared as indicated above) was added and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Solid human tumor sample preparation and lysis:*

Tumor samples were weighed and placed into 50 ml conical tubes and held on ice. Processing was limited to no more than 250 mg tissue per preparation (1 tip/preparation). The protease solution was freshly prepared by diluting into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer (20 ml) was prepared by diluting DNase A to a final concentration of 200 mg/ml (from 100 mg/ml stock). The tumor tissue was homogenated in 19 ml G2 buffer for 60 seconds using the large tip of the polytron in a laminar-flow TC hood in order to avoid inhalation of aerosols, and held at room temperature. Between samples, the polytron was cleaned by spinning at 2 x 30 seconds each in 2L ddH<sub>2</sub>O, followed by G2 buffer (50 ml). If tissue was still present on the generator tip, the apparatus was disassembled and cleaned. Quiagen protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Human blood preparation and lysis:*

Blood was drawn from healthy volunteers using standard infectious agent protocols and citrated into 10 ml samples per tip. Quiagen protease was freshly prepared by dilution into 6.25 ml cold ddH<sub>2</sub>O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer was prepared by diluting RNase A to a final concentration of 200  $\mu$ g/ml from 100 mg/ml stock. The blood (10 ml) was placed into a 50 ml conical tube and 10 ml C1 buffer and 30 ml ddH<sub>2</sub>O (both previously equilibrated to 4°C) were added, and the components mixed by inverting and held on ice for 10 minutes. The nuclei were pelleted with a Beckman swinging bucket rotor at 2500 rpm, 4°C for 15 minutes and the supernatant discarded. With a vortex, the nuclei were suspended into 2 ml C1 buffer (4°C) and 6 ml ddH<sub>2</sub>O (4°C). Vortexing was repeated until the pellet was white. The nuclei were then suspended into the residual buffer using a 200  $\mu$ l tip. G2 buffer (10 ml) were added to the suspended nuclei while gently vortexing, followed by vigorous vortexing for 30 seconds. Quiagen protease was added (200  $\mu$ l) and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (*e.g.*, incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

*Purification of cleared lysates:*(1) Isolation of genomic DNA:

Genomic DNA was equilibrated (1 sample per maxi tip preparation) with 10 ml QBT buffer. QF elution buffer was equilibrated at 50°C. The samples were vortexed for 30 seconds, then loaded onto equilibrated tips and drained by gravity. The tips were washed with 2 x 15 ml QC buffer. The DNA was eluted into 30 ml silanized, autoclaved 30 ml Corex tubes with 15 ml QF buffer (50°C). Isopropanol (10.5 ml) was added to each sample, the tubes covered with parafin and mixed by repeated inversion until the DNA precipitated. Samples were pelleted by centrifugation in the SS-34 rotor at 15,000 rpm for 10 minutes at 4°C. The pellet location was marked, the supernatant discarded, and 10 ml 70% ethanol (4°C) was added. Samples were pelleted again by centrifugation on the SS-34 rotor at 10,000 rpm for 10 minutes at 4°C. The pellet location was marked and the supernatant discarded. The tubes were then placed on their side in a drying rack and dried 10 minutes at 37°C, taking care not to overdry the samples.

After drying, the pellets were dissolved into 1.0 ml TE (pH 8.5) and placed at 50°C for 1-2 hours. Samples were held overnight at 4°C as dissolution continued. The DNA solution was then transferred to 1.5 ml tubes with a 26 gauge needle on a tuberculin syringe. The transfer was repeated 5x in order to shear the DNA. Samples were then placed at 50°C for 1-2 hours.

(2) Quantitation of genomic DNA and preparation for gene amplification assay:

The DNA levels in each tube were quantified by standard  $A_{260}$ ,  $A_{280}$  spectrophotometry on a 1:20 dilution (5  $\mu$ l DNA + 95  $\mu$ l ddH<sub>2</sub>O) using the 0.1 ml quartz cuvetts in the Beckman DU640 spectrophotometer.  $A_{260}/A_{280}$  ratios were in the range of 1.8-1.9. Each DNA samples was then diluted further to approximately 200 ng/ml in TE (pH 8.5). If the original material was highly concentrated (about 700 ng/ $\mu$ l), the material was placed at 50°C for several hours until resuspended.

Fluorometric DNA quantitation was then performed on the diluted material (20-600 ng/ml) using the manufacturer's guidelines as modified below. This was accomplished by allowing a Hoeffer DyNA Quant 200 fluorometer to warm-up for about 15 minutes. The Hoechst dye working solution (#H33258, 10  $\mu$ l, prepared within 12 hours of use) was diluted into 100 ml 1 x TNE buffer. A 2 ml cuvette was filled with the fluorometer solution, placed into the machine, and the machine was zeroed. pGEM 3Zf(+) (2  $\mu$ l, lot #360851026) was added to 2 ml of fluorometer solution and calibrated at 200 units. An additional 2  $\mu$ l of pGEM 3Zf(+) DNA was then tested and the reading confirmed at 400 +/- 10 units. Each sample was then read at least in triplicate. When 3 samples were found to be within 10% of each other, their average was taken and this value was used as the quantification value.

The fluorometrically determined concentration was then used to dilute each sample to 10 ng/ $\mu$ l in ddH<sub>2</sub>O. This was done simultancously on all template samples for a single TaqMan plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with Taqman™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough

for 8-9 plates or 64 tests.

*Gene amplification assay:*

The PRO polypeptide compounds of the invention were screened in the following primary tumors and the resulting  $\Delta C_t$  values greater than or equal to 1.0 are reported in Tables 9A-C below.

Table 9A  
 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO290	PRO341	PRO535	PRO619	PRO1112	PRO809	PRO830	PRO848
LT-1a	—	—	—	—	—	—	1.13	—
LT3	—	—	—	1.04	—	—	—	—
LT7	—	—	—	1.68	—	—	—	—
LT9	—	—	—	1.21	—	—	—	—
LT10	—	—	—	1.34	—	—	—	—
LT11	1.63	—	1.40	1.19	1.135	—	—	—
LT12	—	—	—	1.34	1.525	1.40	1.25	1.04
LT13	1.47	—	1.37	1.41	1.195	1.61	1.35	1.22
LT15	1.67	—	—	2.02	1.635	1.03	—	—
LT16	—	1.12	—	1.69	1.775	—	—	—
LT17	1.22	1.33	1.42	1.57	—	—	—	—
LT18	—	—	—	1.81	1.455	1.10	1.17	—
LT19	2.07	—	—	2.13	1.255	—	—	—
LT21	—	1.15	—	1.74	—	—	1.31	—
CT2	1.56	—	—	2.08	2.265	—	—	—
				1.52				
				—				
				1.83				
				1.67				
				1.32				
				1.14				
				2.33				
				1.90				
				1.15				
				1.09				
				1.22				

Table 9A (cont')  
 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO290	PRO341	PRO535	PRO619	PRO1112	PRO809	PRO830	PRO848
CT3	---	---	1.28	1.49	---	---	---	---
CT8	---	---	---	---	1.065	---	---	---
CT10	---	---	1.34	---	1.575	---	---	---
CT12	---	---	---	---	1.315	---	---	---
CT14	---	---	1.29	---	1.895	---	---	---
CT15	---	---	1.10	1.00	1.465	---	---	---
CT16	---	---	1.35	1.02	1.255	---	---	---
CT17	---	---	1.26	1.23	---	---	---	---
CT1	---	---	---	1.12	1.245	---	---	---
CT4	---	---	1.03	1.25	1.535	---	---	---
CT5	---	---	---	1.34	1.975	---	---	---
CT6	---	---	1.00	1.06	1.575	---	---	---
CT11	1.16	---	1.25	1.80	2.285	---	---	---

Table 9B

ΔCt values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
LT-1	---	1.07	---	---	---	---	---	---	---
LT-1a	---	3.87	---	---	---	---	---	---	---
LT2	---	---	---	---	---	1.23	---	---	---
LT3	---	1.61	---	1.01	---	---	---	1.39	---
LT4	---	---	---	---	---	---	---	1.49	1.01
LT6	---	1.29	---	---	---	---	---	---	---
LT7	---	---	---	---	---	---	---	---	---
LT9	---	2.50	---	---	---	1.21	---	1.58	1.52
LT10	---	---	---	---	---	---	---	1.44	---
LT11	2.06	---	---	---	---	---	---	1.05	---
LT12	1.94	1.21	---	---	---	---	---	1.45	---
LT13	1.64	2.30	---	---	---	---	---	---	---
	1.27	---	---	---	3.84	---	3.55	---	---
LT15	2.05	1.03	---	---	1.01	---	2.47	---	---
LT16	---	1.05	---	---	1.98	---	2.45	---	---
LT17	1.93	---	---	---	---	---	---	1.47	---
LT19	2.90	---	---	---	---	---	---	---	---
LT26	---	---	---	1.66	---	---	---	---	---
LT30	---	---	---	1.58	---	---	---	---	---
CT2	1.92	---	2.00	1.73	---	---	4.75	---	---
	1.70	---	---	---	---	---	---	---	---
CT3	---	---	1.75	---	---	---	1.52	---	---
CT8	1.37	---	1.29	---	---	---	---	---	---
	1.12	---	---	---	---	---	---	---	---



Table 9B (cont')  
 $\Delta$ Ct values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
CT10	2.13	---	1.73	---	---	---	2.82	---	---
	1.67								
CT12	1.43	---	1.92	---	---	---	---	---	---
CT14	1.46	---	2.10	---	---	1.08	1.54	1.38	---
CT15	---	---	2.02	---	1.00	---	---	---	---
CT16	---	---	1.56	---	---	1.11	---	---	---
CT17	1.30	---	1.76	---	---	1.34	---	---	---
CT1	1.36	---	---	---	---	---	1.57	---	---
CT4	---	---	1.06	---	---	---	1.59	---	---
CT5	1.88	---	1.43	---	---	---	---	---	---
	2.51								
CT6	1.41	---	---	---	---	---	---	---	---
	1.75								
CT7	---	---	---	---	---	---	---	1.16	---
CT11	2.80	---	1.83	---	---	---	---	1.17	---
	2.61								
CT18	1.30	---	---	---	---	---	---	1.05	---
H522	---	---	---	---	1.10	---	---	---	---

Table 9C

 $\Delta$ Ct values in lung and colon primary tumors and cell line models

	Primary Tumor	PRO1182	PRO1184	PRO1187	PRO1281
5	LT-1	1.81	---	---	---
	LT-1a	---	1.14	---	---
			1.09		
10	LT4	1.43	1.37	---	---
			1.18		
	LT6	---	1.78	---	---
15			1.66		
			1.05		
	LT9	1.43	---	---	---
20	LT12	---	2.47	1.17	---
			2.61		
			1.80		
25	LT15	---	---	1.55	---
	LT16	---	1.01	1.33	---
	LT17	---	---	---	---
30	LT18	---	1.07	---	---
			1.13		
	LT19	---	1.19	---	---
			1.35		
			1.02		
	LT21	---	1.00	---	---
			1.20		
	CT2	---	---	---	1.15
	CT12	---	---	---	1.07

Because amplification of the various DNAs described above occurs in various cancerous tumors and tumor cell lines derived from various human tissues, these molecules likely play a significant role in tumor formation and/or growth. As a result, amplification and/or enhanced expression of these molecules can serve as a diagnostic for detecting the presence of tumor in an individual and antagonists (*e.g.*, antibodies) directed against the proteins encoded by the above described DNA molecules would be expected to have utility in cancer therapy.

#### EXAMPLE 171: Identification of Receptor/Ligand Interactions

In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparation of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin). Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (*e.g.* Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (*e.g.* FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

Using these assays, the following receptor/ligand interactions have been herein identified:

- (1) PRO943 binds to FHF1, PRO183 (FHF2), PRO184 (FHF3) and PRO185 (FHF4) and vice versa.
- (2) PRO331 binds to PRO1133 and vice versa.
- (3) PRO363 binds to PRO1387 and vice versa.
- (4) PRO5723 binds to PRO1387 and vice versa.
- (5) PRO1114 binds to PRO3301 and PRO9940 and vice versa.
- (6) PRO9828 appears to be a novel fibroblast growth factor receptor (FGFR) ligand in that it binds to the known FGF receptors FGFR1, FGFR2IIIC, FGFR3IIIC and FGFR4. PRO9828 and agonists, therefore, will find use for activating the biological activities normally activated by FGF molecules including, for example, cell growth and proliferation. Antagonists of PRO9828 will find use in blocking the biological activities mediated through the FGF receptor.
- (7) PRO1181 binds to PRO7170, PRO361 and PRO846.

#### EXAMPLE 172: Tissue Expression Distribution

Oligonucleotide probes were constructed from the PRO polypeptide-encoding nucleotide sequences shown in the figures for use in quantitative PCR amplification reactions. The oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human adult and/or fetal tissue sources and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acids in the various tissues tested. Knowledge of the expression pattern or the differential expression of the PRO polypeptide-encoding nucleic acids in various different human tissue types provides a diagnostic marker useful for tissue typing, with or without other tissue-specific markers, for determining the primary tissue source of a metastatic tumor, disease diagnosis, and the like. These assays provided the following results.

<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
DNA16422-1209	substantia nigra, dendrocytes, uterus	hippocampus
DNA16435-1208	substantia nigra, dendrocytes, uterus	hippocampus
DNA26843-1389	dendrocytes, heart, uterus, colon tumor	hippocampus, substantia nigra, cartilage

	<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
	DNA26844-1394	HUVEC, dendrocytes, cartilage	substantia nigra, hippocampus, uterus, prostate
	DNA40621-1440	prostate, uterus, colon tumor	brain, heart, HUVEC, cartilage
5	DNA44161-1434	colon tumor, dendrocytes	substantia nigra, hippocampus, prostate, uterus
	DNA44694-1500	dendrocytes, hippocampus, prostate	colon tumor, substantia nigra, heart
	DNA48320-1433	prostate, uterus	colon tumor, brain, heart, cartilage
	DNA49647-1398	brain, heart, prostate, uterus	cartilage
	DNA53913-1490	hippocampus	substantia nigra, dendrocytes
10	DNA53978-1443	dendrocytes, uterus, prostate	substantia nigra, colon tumor
	DNA53996-1442	spleen, prostate, uterus, hippocampus	substantia nigra, heart
	DNA56050-1455	prostate, uterus, cartilage, hippocampus	heart, colon tumor, dendrocytes
	DNA56110-1437	spleen, colon tumor, brain, prostate	heart
	DNA56410-1414	uterus, dendrocytes	hippocampus, substantia nigra, heart
15	DNA56436-1448	substantia nigra, prostate, hippocampus	dendrocytes, heart, HUVEC
	DNA56855-1447	prostate, uterus	brain, cartilage, heart, colon tumor
	DNA56860-1510	colon tumor	prostate, uterus, dendrocytes
	DNA56868-1478	colon tumor, prostate	uterus, brain, heart, cartilage
	DNA56869-1545	prostate, uterus, cartilage	brain, colon tumor, spleen, heart
20	DNA57699-1412	dendrocytes, hippocampus, prostate	substantia nigra, heart
	DNA57704-1452	brain, heart, spleen, uterus, prostate	colon tumor
	DNA57710-1451	dendrocytes, hippocampus, spleen, uterus	substantia nigra, heart
	DNA57711-1501	dendrocytes, hippocampus, heart, cartilage	substantia nigra
	DNA57827-1493	colon tumor, hippocampus, prostate	substantia nigra, dendrocytes, uterus
25	DNA58723-1588	substantia nigra, cartilage uterus	hippocampus, dendrocytes, HUVEC
	DNA58743-1609	brain, prostate, uterus	colon tumor, heart, spleen, cartilage
	DNA58846-1409	hippocampus, dendrocytes	substantia nigra, uterus, prostate, colon tumor
	DNA58849-1494	prostate	brain, uterus, cartilage, heart, colon tumor
30	DNA58850-1495	spleen, prostate, dendrocytes	hippocampus, substantia nigra, colon tumor
	DNA59213-1487	spleen, cartilage, prostate, substantia nigra	heart, hippocampus, dendrocytes
	DNA59497-1496	dendrocytes, prostate, uterus, heart	cartilage, hippocampus, substantia nigra
35	DNA59605-1418	dendrocytes, prostate, uterus	hippocampus, substantia nigra, colon tumor
	DNA59609-1470	dendrocytes	substantia nigra, hippocampus, heart, prostate, uterus, spleen
40	DNA59612-1466	prostate, dendrocytes	hippocampus, substantia nigra, uterus, colon tumor
	DNA59616-1465	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59619-1464	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59625-1498	brain, colon tumor, prostate, uterus	THP-1 macrophages
45	DNA59827-1426	substantia nigra, prostate, uterus	hippocampus, dendrocytes, heart
	DNA59828-1608	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59853-1505	prostate	brain, uterus, spleen, heart, colon tumor
	DNA59854-1459	cartilage	prostate, brain, heart, colon tumor
50	DNA60283-1484	dendrocytes, spleen, prostate, uterus	hippocampus, substantia nigra, heart
	DNA60619-1482	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA60625-1507	cartilage	prostate, brain, heart, colon tumor
	DNA60629-1481	uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, spleen, prostate
55	DNA61755-1554	dendrocytes, substantia nigra, colon tumor	hippocampus

<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
DNA64852-1589	prostate, uterus	brain, heart, cartilage, colon tumor
DNA66308-1537	prostate, heart uterus	brain, colon tumor, cartilage
DNA68869-1610	spleen, prostate, heart, uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, prostate

5

**EXAMPLE 173: Isolation of cDNA Clones Encoding Human PRO846**

10 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39949. Based on the DNA39949 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO846.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCCTGCAGTGCACCTACAGGGAAG-3' (SEQ ID NO:518)

reverse PCR primer 5'-CTGTCTTCCCCTGCTTGGCTGTGG-3' (SEQ ID NO:519)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39949 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGCAGGAAGGGTGGGATCCTCTTCTCTCGCTGCTCTGGCCACATC-3'

(SEQ ID NO:520)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO846 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO846 [herein designated as DNA44196-1353] (SEQ ID NO:516) and the derived protein sequence for PRO846.

30 The entire nucleotide sequence of UNQ422 (DNA44196-1353) is shown in Figure 329 (SEQ ID NO:516). Clone UNQ422 (DNA44196-1353) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon at nucleotide positions 1021-1023 (Figure 329). The predicted polypeptide precursor is 332 amino acids long (Figure 330). The full-length PRO846 protein shown in Figure 330 has an estimated molecular weight of about 36,143 daltons and a pI of about 5.89. Important regions of the amino acid sequence of PRO846 include the signal peptide, the transmembrane domain, an N-glycosylation site, a sequence typical of fibrinogen beta and gamma chains C-terminal domain, and a sequence typical of Ig like V-type domain as shown in Figure 330. Clone UNQ422 (DNA44196-1353) has been deposited with ATCC and is assigned ATCC deposit no. 209847.

35

**EXAMPLE 174: Isolation of cDNA Clones Encoding Human PRO363**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42828. Based on the DNA42828 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO363.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (42828.f1) 5'-CCAGTGCACAGCAGGCAACGAAGC-3' (SEQ ID NO:521)

reverse PCR primer (42828.r1) 5'-ACTAGGCTGTATGCCTGGGTGGGC-3' (SEQ ID NO:522)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42828 sequence which had the following nucleotide sequence

hybridization probe (42828.p1)

5'-GTATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGC-3' (SEQ ID NO:523)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO363 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO363 [herein designated as UNQ318 (DNA45419-1252)] (SEQ ID NO:500) and the derived protein sequence for PRO363.

The entire nucleotide sequence of UNQ318 (DNA45419-1252) is shown in Figure 313 (SEQ ID NO:500). Clone UNQ318 (DNA45419-1252) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 190-192 and ending at the stop codon at nucleotide positions 1309-1311 (Figure 313). The predicted polypeptide precursor is 373 amino acids long (Figure 314). The full-length PRO363 protein shown in Figure 314 has an estimated molecular weight of about 41,281 daltons and a pI of about 8.33. A transmembrane domain exists at amino acids 221 to 254 of the amino acid sequence shown in Figure 314 (SEQ ID NO:501). The PRO363 polypeptide also possesses at least two myelin P0 protein domains from about amino acids 15 to 56 and from about amino acids 87 to 116. Clone UNQ318 (DNA45419-1252) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209616.

Analysis of the amino acid sequence of the full-length PRO363 polypeptide suggests that it possesses significant sequence similarity to the cell surface protein HCAR, thereby indicating that PRO363 may be a novel HCAR homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO363 amino acid sequence and the following Dayhoff sequences, HS46KDA\_1, HSU90716\_1, MMCARH\_1, MMCARHOM\_1, MMU90715\_1, A33\_HUMAN, P\_W14146, P\_W14158, A42632 and B42632.

**EXAMPLE 175: Isolation of cDNA Clones Encoding a Human PRO9828**

A consensus DNA sequence was assembled relative to other nucleic sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA139814. Based on the DNA139814 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO9828. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

5'-AATCTCAGCACCAGCCACTCAGAGCA-3' (SEQ ID NO:524)

5'-GTTAAAGAGGGTGCCCTTCCAGCGA-3' (SEQ ID NO:525)

5'-TATCCCAATGCCTCCCCACTGCTC-3' (SEQ ID NO:526)

5'-GATGAACTTGGCGAAGGGGCGGCA-3' (SEQ ID NO:527)

RNA for construction of the cDNA libraries was isolated from human fetal liver tissue. The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for a full-length PRO9828 polypeptide (designated herein as DNA142238-2768 [Figure 323, SEQ ID NO:510]) and the derived protein sequence for that PRO9828 polypeptide.

The full length clone identified above contained a single open reading frame with an apparent translational initiation site at nucleotide positions 232-234 and a stop signal at nucleotide positions 985-987 (Figure 323, SEQ ID NO:510). The predicted polypeptide precursor is 251 amino acids long, has a calculated molecular weight of approximately 27,954 daltons and an estimated pI of approximately 9.22. Analysis of the full-length PRO9828 sequence shown in Figure 324 (SEQ ID NO:511) evidences the presence of a variety of important polypeptide domains as shown in Figure 324, wherein the locations given for those important polypeptide domains are approximate as described above. Chromosome mapping evidences that the PRO9828-encoding nucleic acid maps to chromosome 12p13 in humans. Clone DNA142238-2768 has been deposited with ATCC on October 5, 1999 and is assigned ATCC deposit no. 819-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 324 (SEQ ID NO:511), evidenced sequence



identity between the PRO9828 amino acid sequence and the following Dayhoff sequences: P\_Y08581, AB018122\_1, FGF3\_HUMAN, P\_R70824, S54407, P\_R80780, P\_Y23761, P\_W92312, OMFGF6\_1 and P\_R80871.

**EXAMPLE 176: Isolation of cDNA Clones Encoding a Human PRO7170**

5 DNA108722-2743 was identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., Genbank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals.

15 Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, designated herein as CLU57836. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., Genbank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58756.

20 In light of an observed sequence homology between the DNA58756 sequence and an EST sequence encompassed within clone no. 2251462 from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, clone no. 2251462 was purchased and the cDNA insert was obtained and sequenced. It was found herein that that cDNA insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 325 and is herein designated as DNA108722-2743.

30 Clone DNA108722-2743 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon at nucleotide positions 1506-1508 (Figure 325). The predicted polypeptide precursor is 482 amino acids long (Figure 326). The full-length PRO7170 protein shown in Figure 326 has an estimated molecular weight of about 49,060 daltons and a pI of about 4.74. Analysis of the full-length PRO7170 sequence shown in Figure 326 (SEQ ID NO:513) evidences the presence of a variety of important polypeptide domains as shown in Figure 326, wherein the locations given for those important polypeptide domains are approximate as described above. Clone DNA108722-2743 has been

deposited with ATCC on August 17, 1999 and is assigned ATCC Deposit No. 552-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 326 (SEQ ID NO:513), evidenced sequence identity between the PRO7170 amino acid sequence and the following Dayhoff sequences: P\_Y12291, I47141, D88733\_1, DMC56G7\_1, P\_Y11606, HWP1\_CANAL, HSMUC5BEX\_1, HSU78550\_1, HSU70136\_1, and SGS3\_DROME.

#### EXAMPLE 177: Isolation of cDNA Clones Encoding Human PRO361

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40654. Based on the DNA40654 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO361.

Forward and reverse PCR primers were synthesized as follows:

<u>forward PCR primer</u>	5'-AGGGAGGATTATCCTTGACCTTTGAAGACC-3'	(SEQ ID NO:528)
<u>forward PCR primer</u>	5'-GAAGCAAGTGCCAGCTC-3'	(SEQ ID NO:529)
<u>forward PCR primer</u>	5'-CGGGTCCCTGCTCTTTGG-3'	(SEQ ID NO:530)
<u>reverse PCR primer</u>	5'-CACCGTAGCTGGGAGCGCACTCAC-3'	(SEQ ID NO:531)
<u>reverse PCR primer</u>	5'-AGTGTAAGTCAAGCTCCC-3'	(SEQ ID NO:532)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40654 sequence which had the following nucleotide sequence

hybridization probe

5'- GCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATTGCCTCAAAAAGAG-3' (SEQ ID NO:533)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO361 gene using the probe oligonucleotide. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO361 [herein designated as DNA45410-1250] (SEQ ID NO:514) and the derived protein sequence for PRO361.

The entire nucleotide sequence of DNA45410-1250 is shown in Figure 327 (SEQ ID NO:514). Clone DNA45410-1250 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 226-228 and ending at the stop codon at nucleotide positions 1519-1521 (Figure 327). The predicted polypeptide precursor is 431 amino acids long (Figure 328). The full-length PRO361 protein shown in Figure 328 has an estimated molecular weight of about 46,810 daltons and a pI of about 6.45. In addition, regions of interest including the transmembrane domain (amino acids 380-409) and sequences typical of the arginase family of proteins (amino acids 3-14 and 39-57) are designated in Figure 328. Clone DNA45410-1250 has been deposited with ATCC and is assigned ATCC deposit no. ATCC 209621.

Analysis of the amino acid sequence of the full-length PRO361 polypeptide suggests that portions of it possess significant homology to the mucin and/or chitinase proteins, thereby indicating that PRO361 may be a novel mucin and/or chitinase protein.

EXAMPLE 178: Isolation of cDNA Clones Encoding a Human PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940

DNA molecules encoding the PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940 polypeptides shown in the accompanying figures were obtained through GenBank.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 10

	<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
15	DNA45410-1250	209621	February 5, 1998
	DNA108722-2743	552-PTA	August 17, 1999
	DNA142238-2768	819-PTA	October 5, 1999
	DNA40981-1234	209439	November 7, 1997
	DNA45419-1252	209616	February 5, 1998
20	DNA44196-1353	209847	May 6, 1998
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
25	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
30	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
35	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
40	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
	DNA49820-1427	209932	June 2, 1998
45	DNA49821-1562	209981	June 16, 1998
	DNA52192-1369	203042	July 1, 1998
	DNA52598-1518	203107	August 11, 1998
	DNA53913-1490	203162	August 25, 1998

Table 10 (cont')

	DNA53978-1443	209983	June 16, 1998
	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
5	DNA56050-1455	203011	June 23, 1998
	DNA56110-1437	203113	August 11, 1998
	DNA56113-1378	203049	July 1, 1998
	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448	209902	May 27, 1998
10	DNA56855-1447	203004	June 23, 1998
	DNA56859-1445	203019	June 23, 1998
	DNA56860-1510	209952	June 9, 1998
	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342	203023	June 23, 1998
15	DNA56868-1209	203024	June 23, 1998
	DNA56869-1545	203161	August 25, 1998
	DNA56870-1492	209925	June 2, 1998
	DNA57033-1403	209905	May 27, 1998
	DNA57037-1444	209903	May 27, 1998
20	DNA57129-1413	209977	June 16, 1998
	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57694-1341	203017	June 23, 1998
	DNA57695-1340	203006	June 23, 1998
25	DNA57699-1412	203020	June 23, 1998
	DNA57702-1476	209951	June 9, 1998
	DNA57704-1452	209953	June 9, 1998
	DNA57708-1411	203021	June 23, 1998
	DNA57710-1451	203048	July 1, 1998
30	DNA57711-1501	203047	July 1, 1998
	DNA57827-1493	203045	July 1, 1998
	DNA57834-1339	209954	June 9, 1998
	DNA57836-1338	203025	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
35	DNA57844-1410	203010	June 23, 1998
	DNA58721-1475	203110	August 11, 1998
	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 18, 1998
	DNA58743-1609	203154	August 25, 1998
40	DNA58846-1409	209957	June 9, 1998
	DNA58848-1472	209955	June 9, 1998
	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 9, 1998
	DNA58853-1423	203016	June 23, 1998
45	DNA58855-1422	203018	June 23, 1998
	DNA59205-1421	203009	June 23, 1998
	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	June 9, 1998
	DNA59214-1449	203046	July 1, 1998
50	DNA59215-1425	209961	June 9, 1998
	DNA59220-1514	209962	June 9, 1998
	DNA59488-1603	203157	August 25, 1998
	DNA59493-1420	203050	July 1, 1998
	DNA59497-1496	209941	June 4, 1998
55	DNA59588-1571	203106	August 11, 1998

Table 10 (cont')

	DNA59603-1419	209944	June 9, 1998
	DNA59605-1418	203005	June 23, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
5	DNA59609-1470	209963	June 9, 1998
	DNA59610-1559	209990	June 16, 1998
	DNA59612-1466	209947	June 9, 1998
	DNA59613-1417	203007	June 23, 1998
	DNA59616-1465	209991	June 16, 1998
10	DNA59619-1464	203041	July 1, 1998
	DNA59620-1463	209989	June 16, 1998
	DNA59625-1498	209992	June 17, 1998
	DNA59767-1489	203108	August 11, 1998
	DNA59776-1600	203128	August 18, 1998
15	DNA59777-1480	203111	August 11, 1998
	DNA59820-1549	203129	August 18, 1998
	DNA59827-1426	203089	August 4, 1998
	DNA59828-1608	203158	August 25, 1998
	DNA59838-1462	209976	June 16, 1998
20	DNA59839-1461	209988	June 16, 1998
	DNA59841-1460	203044	July 1, 1998
	DNA59842-1502	209982	June 16, 1998
	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
25	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
30	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
35	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
40	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
45	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
50	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
	DNA71159-1617	203135	August 18, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28),  
5 Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure  
10 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure  
15 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure  
20 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure  
30 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure  
35 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure

284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID



NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure

181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 10.

5. A vector comprising the nucleic acid of Claim 1.

6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7 wherein said cell is a CHO cell.

9. The host cell of Claim 7 wherein said cell is an *E. coli*.

10. The host cell of Claim 7 wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID

NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 10.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

20. The antibody of Claim 17 wherein said antibody is an antibody fragment.

21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50

(SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46),  
5 Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure  
10 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure  
15 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure  
20 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure  
25 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure  
30 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure  
35 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure

293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

23. An isolated extracellular domain of of PRO polypeptide.

24. An isolated PRO polypeptide lacking its associated signal peptide.

25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.

26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

27. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure

169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID



NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure

90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

28. An isolated polypeptide having at least 80% amino acid sequence identity to:
- (a) the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36),

Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID

NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID

NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure

254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

29. A method of detecting a PRO943 polypeptide in a sample suspected of containing a PRO943 polypeptide, said method comprising contacting said sample with a PRO183, PRO184 or PRO185 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO943 polypeptide in said sample.

30. The method according to Claim 29, wherein said sample comprises cells suspected of expressing said PRO943 polypeptide.

31. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is labeled with a detectable label.

32. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is attached to a solid support.

33. A method of detecting a PRO183, PRO184 or PRO185 polypeptide in a sample suspected of containing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said sample with a PRO943 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO183, PRO184 or PRO185 polypeptide in said sample.

34. The method according to Claim 33, wherein said sample comprises cells suspected of expressing said PRO183, PRO184 or PRO185 polypeptide.

35. The method according to Claim 33, wherein said PRO943 polypeptide is labeled with a detectable label.

36. The method according to Claim 33, wherein said PRO943 polypeptide is attached to a solid support.

37. A method of detecting a PRO331 polypeptide in a sample suspected of containing a PRO331 polypeptide, said method comprising contacting said sample with a PRO1133 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO331 polypeptide in said sample.

38. The method according to Claim 37, wherein said sample comprises cells suspected of expressing said PRO331 polypeptide.

39. The method according to Claim 37, wherein said PRO1133 polypeptide is labeled with a detectable label.

40. The method according to Claim 37, wherein said PRO1133 polypeptide is attached to a solid support.

41. A method of detecting a PRO1133 polypeptide in a sample suspected of containing a PRO1133 polypeptide, said method comprising contacting said sample with a PRO331 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1133 polypeptide in said sample.

42. The method according to Claim 41, wherein said sample comprises cells suspected of expressing said PRO1133 polypeptide.

43. The method according to Claim 41, wherein said PRO331 polypeptide is labeled with a detectable label.

44. The method according to Claim 41, wherein said PRO331 polypeptide is attached to a solid support.

45. A method of detecting a PRO363 or PRO5723 polypeptide in a sample suspected of containing a PRO363 or PRO5723 polypeptide, said method comprising contacting said sample with a PRO1387 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO363

or PRO5723 polypeptide in said sample.

46. The method according to Claim 45, wherein said sample comprises cells suspected of expressing said PRO363 or PRO5723 polypeptide.

5 47. The method according to Claim 45, wherein said PRO1387 polypeptide is labeled with a detectable label.

48. The method according to Claim 45, wherein said PRO1387 polypeptide is attached to a solid support.

10 49. A method of detecting a PRO1387 polypeptide in a sample suspected of containing a PRO1387 polypeptide, said method comprising contacting said sample with a PRO363 or PRO5723 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1387 polypeptide in said sample.

15 50. The method according to Claim 49, wherein said sample comprises cells suspected of expressing said PRO1387 polypeptide.

20 51. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is labeled with a detectable label.

52. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is attached to a solid support.

25 53. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO3301 or PRO9940 polypeptide and determining the formation of a PRO1114/PRO3301 or PRO9940 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

30 54. The method according to Claim 53, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

35 55. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is labeled with a detectable label.



56. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is attached to a solid support.

57. A method of detecting a PRO3301 or PRO9940 polypeptide in a sample suspected of containing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO3301 or PRO9940/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO3301 or PRO9940 polypeptide in said sample.

58. The method according to Claim 57, wherein said sample comprises cells suspected of expressing said PRO3301 or PRO9940 polypeptide.

59. The method according to Claim 57, wherein said PRO1114 polypeptide is labeled with a detectable label.

60. The method according to Claim 57, wherein said PRO1114 polypeptide is attached to a solid support.

61. A method of detecting a PRO1181 polypeptide in a sample suspected of containing a PRO1181 polypeptide, said method comprising contacting said sample with a PRO7170, PRO361 or PRO846 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1181 polypeptide in said sample.

62. The method according to Claim 61, wherein said sample comprises cells suspected of expressing said PRO1181 polypeptide.

63. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is labeled with a detectable label.

64. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is attached to a solid support.

65. A method of detecting a PRO7170, PRO361 or PRO846 polypeptide in a sample suspected of containing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said sample with a PRO1181 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO7170, PRO361 or PRO846 polypeptide in said sample.

66. The method according to Claim 65, wherein said sample comprises cells suspected of expressing said PRO7170, PRO361 or PRO846 polypeptide.

67. The method according to Claim 65, wherein said PRO1181 polypeptide is labeled with a detectable label.

68. The method according to Claim 65, wherein said PRO1181 polypeptide is attached to a solid support.

69. A method of linking a bioactive molecule to a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

70. The method according to Claim 69, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

71. The method according to Claim 69, wherein said bioactive molecule causes the death of said cell.

72. A method of linking a bioactive molecule to a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

73. The method according to Claim 72, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

74. The method according to Claim 73, wherein said bioactive molecule causes the death of said cell.

75. A method of linking a bioactive molecule to a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

76. The method according to Claim 75, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

77. The method according to Claim 75, wherein said bioactive molecule causes the death of said cell.

78. A method of linking a bioactive molecule to a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

79. The method according to Claim 78, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

80. The method according to Claim 78, wherein said bioactive molecule causes the death of said cell.

81. A method of linking a bioactive molecule to a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

82. The method according to Claim 81, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

83. The method according to Claim 81, wherein said bioactive molecule causes the death of said cell.

84. A method of linking a bioactive molecule to a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

85. The method according to Claim 84, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

86. The method according to Claim 84, wherein said bioactive molecule causes the death of said cell.

87. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

5 88. The method according to Claim 87, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

89. The method according to Claim 87, wherein said bioactive molecule causes the death of said cell.

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90. A method of linking a bioactive molecule to a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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91. The method according to Claim 90, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

20 92. The method according to Claim 90, wherein said bioactive molecule causes the death of said cell.

25 93. A method of linking a bioactive molecule to a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

94. The method according to Claim 93, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

30 95. The method according to Claim 93, wherein said bioactive molecule causes the death of said cell.

35 96. A method of linking a bioactive molecule to a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

97. The method according to Claim 96, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

98. The method according to Claim 96, wherein said bioactive molecule causes the death of said cell.

99. A method of modulating at least one biological activity of a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide or an anti-PRO943 antibody, whereby said PRO183, PRO184 or PRO185 polypeptide or said anti-PRO943 antibody binds to said PRO943 polypeptide, thereby modulating at least one biological activity of said cell.

100. The method according to Claim 99, wherein said cell is killed.

101. A method of modulating at least one biological activity of a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide or an anti-PRO183, anti-PRO184 or anti-PRO185 antibody, whereby said PRO943 polypeptide or said anti-PRO183, anti-PRO184 or anti-PRO185 antibody binds to said PRO183, PRO184 or PRO185 polypeptide, thereby modulating at least one biological activity of said cell.

102. The method according to Claim 101, wherein said cell is killed.

103. A method of modulating at least one biological activity of a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide or an anti-PRO331 antibody, whereby said PRO1133 polypeptide or said anti-PRO331 antibody binds to said PRO331 polypeptide, thereby modulating at least one biological activity of said cell.

104. The method according to Claim 103, wherein said cell is killed.

105. A method of modulating at least one biological activity of a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide or an anti-PRO1133 antibody, whereby said PRO331 polypeptide or said anti-PRO1133 antibody binds to said PRO1133 polypeptide, thereby modulating at least one biological activity of said cell.

106. The method according to Claim 105, wherein said cell is killed.

107. A method of modulating at least one biological activity of a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide or an anti-PRO1387 antibody, whereby said PRO363 or PRO5723 polypeptide or said anti-PRO1387 antibody binds to said PRO1387 polypeptide, thereby modulating at least one biological activity of said cell.

5 108. The method according to Claim 107, wherein said cell is killed.

109. A method of modulating at least one biological activity of a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide or an anti-PRO363 or anti-PRO5723 antibody, whereby said PRO1387 polypeptide or said anti-PRO363 or anti-PRO5723 antibody binds to said PRO363 or PRO5723 polypeptide, thereby modulating at least one biological activity of said cell.

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110. The method according to Claim 109, wherein said cell is killed.

111. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide or an anti-PRO1114 antibody, whereby said PRO3301 or PRO9940 polypeptide or said anti-PRO1114 antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.

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20 112. The method according to Claim 111, wherein said cell is killed.

113. A method of modulating at least one biological activity of a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO3301 or anti-PRO9940 antibody, whereby said PRO1114 polypeptide or said anti-PRO3301 or anti-PRO9940 antibody binds to said PRO3301 or PRO9940 polypeptide, thereby modulating at least one biological activity of said cell.

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114. The method according to Claim 113, wherein said cell is killed.

115. A method of modulating at least one biological activity of a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide or an anti-PRO1181 antibody, whereby said PRO7170, PRO361 or PRO846 polypeptide or said anti-PRO1181 antibody binds to said PRO1181 polypeptide, thereby modulating at least one biological activity of said cell.

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35 116. The method according to Claim 115, wherein said cell is killed.

117. A method of modulating at least one biological activity of a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide or an anti-PRO7170, anti-PRO361 or anti-PRO846 antibody, whereby said PRO1181 polypeptide or said anti-PRO7170, anti-PRO361 or anti-PRO846 antibody binds to said PRO7170, PRO361 or PRO846 polypeptide, thereby modulating at least one biological activity of said cell.

5

118. The method according to Claim 117, wherein said cell is killed.

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**FIGURE 1**

CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTTCAGATCTGCTCGGTAGA  
CCTGGTGCACCACCACCATGTTGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG  
GTTTTCCACCCAGCTTTCACCAAGGCCTCCCCTGTTGTGAAGAATTCATCACAAGAATCA  
ATGGCTGTTAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA  
GAACTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAATATTTAAAATT  
GATCAGATGGGAAGATGGTTTGTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA  
CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT  
ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAACAGCT  
TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG  
GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC  
CATATGACCAGAGCCCAGGCCCAAAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT  
GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCTCTTCTCATCAGAGCTGCATGGTACAC  
AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCAGTGAAAAGTTTCTGA  
ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCTCATTGGGATCTATG  
TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT  
AGTTCCTTTTCAGCATGTTCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAAGTAT  
CACCAATGTATGGAGTTCAAAAATATGATCCATTAACTCGATGCTGAGTATCTACATGGAT  
ACATTAAATATATTTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAGAATC  
AAGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTAATGGGGCAGATATGC  
ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA  
TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTCTGGAGAATAAATGCAGT  
AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT  
TTGGTGAATGTGAAAACATAAAGTTTGTGTCATGAGAATGTAAGTCTTTTTTCTACTTTAAAA  
TTTAGTAGGTTCACTGAGTAACTAAAATTTAGCAAACCTGTGTTTGCATATTTTTTTGGAGT  
GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTGGTAAAGGGACCAGACAGAAG  
GAGTCACCTGCAGTCTTTTGTTTTTTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA  
GTGAGGAGCCAGTAAGAAACATCTGGGTATTTGGAAACAAGTGGTCATTGTTACATTCATTT  
GCTGAACTTAACAAAACCTGTTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG  
CTTCTCAGTGCTCTCTTTCCAATATAGATGTGGTCATGTTTGACTTGTACAGAATGTTAATC  
ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA  
ATAACTTTAAAACATTTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG  
AATACAAACAGTATACTCATG



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**FIGURE 2**

MLAARLVCLRTLPSRVFHPAFTKASPVVKN SITKNQWLLTPSREYATKTRIGIRRGRTGQEL  
KEAALEPSMEKIFKIDQMGRW FVAGGA AVGLGALCY YGLGLSNEIGAIEKAVIWPQYVKDRI  
HSTYMYLAGSIGLTALSAIAIS RTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP  
GPKHLAWLLHSGVMGAVVAPL TILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL  
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLF SMFLLYDTQKVIKRAEVSPMYGV  
QKYDPINSMLSIYMDTLNIFMRVATMLATGGNRKK

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**FIGURE 3**

GAAGGCTGCCTCGCTGGTCCGAATTCGGTGGCGCCACGTCCGCCCCGTCTCCGCCTTCTGCAT  
CGCGGGCTTCGGCGGGCTTCCACCTAGACACCTAACAGTCGCGGAGCCGGCCGCGTCGTGAGGG  
GGTCGGCACGGGGAGTCGGGCGGTCTTGTGCATCTTGGGTACCTGTGGGTCTGAAGATGTTCGG  
ACATCGGAGACTGGTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTTCGCCGCCACCGTC  
GCCGTGCCCTTGGTCGGCAAACTCGGCCCTCATCAGCCCGGCCCTACCTCTTCCCTCTGGCCCCGA  
AGCCTTCCCTTTATCGCTTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG  
GTCCAGGAAGTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTCTACGCGA  
CTTGAAACAGGAGCTTTTGATGGGAGGCCAGCAGACTATTTATTCATGCTCCTCTTTAACTG  
GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA  
TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGGA  
ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG  
CTCGGTAAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTTCCCTAATGTTCA  
GATACCCAATGGACTTGGGAGGAAGAAATTTCTATCCACACCTCAGTTTTTGTACCGCTGG  
CTGCCCCAGTAGGAGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC  
TGCTGATCAGAATGGCGGAGGCGGGAGACACAACCTGGGGCCAGGGCTTTCGACTTGGAGACC  
AGTGAAGGGGCGGCCTCGGGCAGCCGCTCCTCTCAAGCCACATTTCCCTCCAGTGCTGGGTG  
CACTTAACAACCTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC  
AGTACGAGACAAAGTTTCTTAAATCCCAGAAAAATATAAGTGTTCCACAAGTTTTCACGAT  
TCTCATTTCAAGTCCTTACTGCTGTGAAGAACAATAACCAACTGTGCAAAATTGCAAACTGAC  
TACATTTTTTGGTGTCTTCTCTTCTCCCCTTTCCGTCTGAATAATGGGTTTTAGCGGGTCTCT  
AATCTGCTGGCATTGAGCTGGGGCTGGGTACCAAACCCTTCCCAAAAGGACCTTATCTCTT  
TCTTGACACATGCCTCTCTCCCCTTTTCCCAACCCCCACATTTGCAACTAGAAAAAGTTG  
CCCATAAAAATTGCTCTGCCCTTGACAGGTTCTGTTATTTATTGACTTTTGCCAAGGCTGGTC  
ACAACAATCATATTCACGTTATTTTCCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG  
AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGGAAATTGCTTCGACTGACATCCGTTGTT  
AACCCTTTGCCACTCTTCAGATATTTTTTATAAAAAAAGTACCACTGAGTTCATGAGGGCCA  
CAGATTGGTTATTAATGAGATACGAGGGTTGGTGTGCTGGGTGTTTGTTCCTGAGCTAAGTGA  
TCAAGACTGTAGTGGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC  
TTTGCGTTTCATATGTAGCCCTACTGGCTTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT  
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTTGAGAGGTCCTGGGCATTG  
ATTCCCATTTCATCTCATTCTGGATATGTGTTTATTGAGTAAAGGAGGAGAGACCCTCATA  
CGCTATTTTAAATGTCACTTTTTTGCCTATCCCCCGTTTTTTGGTCATGTTTCAATTAATTGT  
GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA  
AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAGGGTGTGTTA  
TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTT  
TCGTAGGTGGGCTTTTCCCTATCAGAGCTTGGCTCATAACCAATAAAGTTTTTGAAGGCCA  
TGGCTTTTTCACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT  
ATTGAGTGGCTGTCACACTTTGAGGCAACTAAAAAGGCTTCAAACGTTTTGATCAGTTTCTT  
TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTCCCCCACTCTTAAACAGTGTGAT  
GTGTGTTATCTAGGAAATGAGAGTTGGCAACAACCTCTCATTTTGAATAGAGTTTGTGTG  
TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGGAGAGTCTGAACCTTAACTGTCA  
TGTTTTGTTGTTTCATCTGTGGCCACAATAAAGTTTACTTGTAAAATTTTAGAGGCCATTACT  
CCAATTATGTTGCACGTACACTCATTGTACAGGCGTGGAGACTCATTGTATGTATAAGAATA  
TTTCTGACAGTGAGTGACCCGGAGTCTCTGGTGTACCTCTTACCAGTCAGCTGCCTGCGAG  
CAGTCATTTTTTCCCTAAAGTTTTACAAGTATTTAGAAGTTTTCAGTTCAGGGCAAAATGTTT  
ATGAAGTTATTCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT  
ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA  
TGACAGTGGATTCTCTTTACAAATGGAAAAAATAATCCTTATTTTGTATAAAGGACTTCCC  
TTTTTGTAACCTAATCCTTTTTTATTGGTAAAAATTGTAAATTAATGTGCAACTTG

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**FIGURE 4**

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGGLISPAYLFLWPEAFLYRFQIWRPITATFYF  
PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP  
LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNLVGHLYFFL  
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRL  
GDQ

**Transmembrane domain:**

amino acids 98-116, 152-172

**N-myristoylation site.**

amino acids 89-95, 168-174, 176-182, 215-221, 221-227, 237-243

**Glycosaminoglycan attachment site.**

amino acids 218-222

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**FIGURE 5**

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTTGCCATAGCGACCATTTTGCATTAAGTGGTTG  
GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT  
CCTTGTGGCCCCAAAGGCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC  
CCTTTGGGGCGGGATGGCTGCGGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG  
CGGGGTTCCCTGCGAGGCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT  
GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT  
GGCCTGTGTTCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTC  
ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT  
AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC  
CATTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA  
AAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTACCT  
GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT  
GAGGGAAGTTCTTAGAAAATCAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA  
AACAGTTATCAGAGGCTAAAACAGAAGAGCCCACAGTGCACTCCAGTGAAGCTGCAATAATG  
AATAATTCCCAAGGGGATGGTGAACATTTTGCACACCCACCCTCAGAAGTTAAAATGCATTT  
TGCTAATCAGTCAATAGAACCTTTGGGAAGAAAAGTGGAAGGTCTGAAACTTCCTCCCTCC  
CACAAAAGGCCTGAAGATTCCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC  
TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA  
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG  
GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG  
CAAACATTACTAAAGAGGAGATTGCTTGACAGAGAACTCAAAGAAGAAGTTATTAATAAGTA  
ATAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTC  
CTTACACTG

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**FIGURE 6**

MAAEEDEVEWVVESIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP  
LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEAactsPLAKTHTSQAILQP  
VLAEDFTIFKAMMVQKNIEMLQAIIRIIQERNGLPDCLTDGSDVSDLEHEEMKILREVL  
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS  
IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLMS  
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAAEEKQTLLKRRLLAEKLKEEVINK

**N-glycosylation sites.**

amino acids 224-228, 246-250, 285-289

**N-myristoylation site.**

amino acids 273-279

**Amidation site.**

amino acids 252-256

**Cytosolic fatty-acid binding proteins.**

amino acids 78-108

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**FIGURE 7**

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT  
TCATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA  
TTAATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAG  
GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC  
AGAAAAACATTGAAATGCAGCTGCAAGCCATTCGAATAATTCAAGAGAGAAATGGTGTATTA  
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT  
CCTGAGGGAAGTTCTTAGAAAATCAAAGAGGAATATGACCAGGAA

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**FIGURE 8**

GCGTGGTTTTTGTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTTCGCCTATACCTACTG  
TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG  
TCTCAGCTCTAGGATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTA AAAAAC  
AGTGGAATGGAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATAC  
ATTCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT  
CTGCCAATGAAGAAAAACAAGTATGATTATCTTCCAACCTACTGTGAATGTGTGCTCAGAACTG  
GTGAAGCTAGTTTTCTGTGTGCTTGTGTCACTTCTGTGTTATAAAGAAAGATCATCAAAGTAG  
AAATTTGAAATATGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCTGCCT  
TTCTTTATTTCTGGATAACTTGATTGTCTTCTATGTCTGCTATCTTCAACCAGCCATG  
GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAA  
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCT  
TGACTGCCGGGACTAAAACCTTTACAGCACAACTTGGCAGGACGTGGATTTTCATCACGATGCC  
TTTTTCAGCCCTTCCAATTCCTGCCTTCTTTTCAGAAAGTGAGTGTCCAGAAAAGACAATTG  
TACAGCAAAGGAATGGACTTTTCTGAAGCTAAATGGAACACCACAGCCAGAGTTTTTCAGTC  
ACATCCGTCTTGGCATGGGCCATGTTCTTATTATAGTCCAGTGTTTTATTCTTCAATGGCT  
AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA  
GAACAGCAAACCTCTATTTCTTTGGCATTCTGTTAATGGGCTGACTCTGGGCCTTCAGAGGA  
GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTTATGGCCACAGTGCATTTTCAGTAGCC  
CTTATTTTTGTAACCTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA  
CATGTTCCATGTCTTGATGGCCAGGTTACCACTGTCATTATCACAACAGTGTCTGTCTCTGG  
TCTTTGACTTCAGGCCCTCCCTGGAATTTTTCTTGGAAAGCCCCATCAGTCTTCTCTCTATA  
TTTATTATAAGTCCAGCAAGCCTCAAGTTCGGGAATACGCACCTAGGCAAGAAAGGATCCG  
AGATCTAAGTGGCAATCTTTGGGAGCGTTCAGTGGGGATGGAGAAGAACTAGAAAGACTTA  
CCAAACCCAAGAGTGATGAGTCAGATGAAGATACTTTCTAACTGGTACCCACATAGTTTGCA  
GCTCTCTTGAACCTTATTTTCACATTTTCAGTGTTTGTAAATATTTATCTTTTCACTTTGATA  
AACCAGAAATGTTTCTAAATCCTAATATTCTTTGCATATATCTAGCTACTCCCTAAATGGTT  
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA  
ATATGAAGAATTCATTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT  
TTTCTTGGCCTTCAAGCTTCCAAAAAAGCTTGTAAATCATGTTAGCTATAGCTTGTATAT  
ACACATAGAGATCAATTTGCCAAATATTCACAATCATGTAGTTCTAGTTTACATGCCAAAGT  
CTTCCCTTTTTTAACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT  
CATTTTGAAGTAAAGAGCAACGGGACCCTTTCTAAAAACGTTGGTTGAAGGACCTAAATAC  
CTGGCCATACCATAGATTTGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT  
TTCTCAGACACAACATCTCAGAATTTTAATTTTTTAGAAATTCATGGGAAATTGGATTTTTGT  
AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACCACTTGTATTTTA  
AGTCATTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT  
GTCATTACTCCTGAATTATTACATTTTGGAGAATAAGAGGGCATTTTATTTTATTAGTTACT  
AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATA  
CAGATTGTGCTGAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAGGATCACTT  
AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC  
AGTAATATATAAGTCACTTTACAGTGCTACTTCACACTTAAAAGTGCATGGTATTTTTTCATG  
GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA  
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG  
CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT  
CATTTCTCAGAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA  
AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG  
GTGGAAATTTGTAATTAATAATTATTAAACCT

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**FIGURE 9**

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK  
LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAV  
IFS NFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF  
SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI  
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSASFVALI  
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI  
YNASKPQVPEYAPRQERIRDLSGNLWERSSSGDGEELERLTKPKSDESDETF

**Transmembrane domains:**

amino acids 16-36 (type II), 50-74, 147-168, 229-250, 271-293,  
298-318, 328-368

**N-glycosylation sites.**

amino acids 128-132, 204-208, 218-222, 374-378

**Glycosaminoglycan attachment site.**

amino acids 402-406

**N-myristoylation sites.**

amino acids 257-263, 275-281, 280-286, 284-290, 317-323



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**FIGURE 10**

CGTGCCTGCGCAATGGGTGTCGGGTCCGCTTTTTCCCAATCCGGACGTAATCGTGGTTTTTG  
TTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTGTAGCTTCTCCAC  
GTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTCAGCTCTAG  
GATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAAAAACAGTGGAATGGAA  
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCACAATGTATACATTCCTGCTAGG  
TGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATTCTGCCAATGAAG  
AAAACAAGTATGATTATCTTCCAACACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT  
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAAGAAAGATCATCAAAGTAGAAATTTGAAATA  
TGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCTGCCTTTCTTTATTTCC  
TGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATGGCTGTTATCTTC  
TCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAAGAGGCGTCTAAA  
CTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCTTGACTGCCGGGA  
CTAAAACTTTA

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**FIGURE 11**

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGCCGGCTTGGCTAGCGCGCGGCGGCC  
GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT  
CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG  
AGCGGCTCCGCGGCGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCCGGCCCA  
GGTGAAGAAAGAACCGAAAAAGAAGAAACAACAGTTGTCTGTTTGCAACAAGCTTTGCTATG  
CACTTGGGGGAGCCCCCTACCAGGTGACGGGCTGTGCCCTGGGTTTCTTCCTTCAGATCTAC  
CTATTGGATGTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC  
CTGGGATGCCATCACAGACCCCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC  
TGGGTGCGCTTATGCCCTGGATCATCTTCTCCACGCCCCTGGCCGTCATTGCCTACTTCCTC  
ATCTGGTTGCTGCCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT  
CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTTCATCAGCA  
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC  
AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTCAGG  
ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATAACATGGCACCCTTCACAC  
AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTG  
TGCTGTATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTG  
AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATAACATAAATT  
ATTACTGGCTTCTCTTACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACCTTTGTCTTGTT  
TTGACCTACACTTGGGCTTCCGCAATGAATCCAGAATCTACTCCTGGCCATCATGCTCT  
CGGCCACTTTAACCATTCCCATCTGGCAGTGTTCTTGACCCGGTTTGGCAAGAAGACAGCT  
GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA  
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC  
TACCCTGGTCCATGCTGCCTGATGTATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT  
GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTCACCAAGTTTGCCTCTGGAGTGTC  
ACTGGGCATTTCTACCCTCAGTCTGGACTTTGCAGGGTACCAGACCCGTGGCTGCTCGCAGC  
CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG  
CTGGGCCTGCTGCTCTTCAAAATGTACCCCATTGATGAGGAGAGGCGGCGGAGAGAAAGAA  
GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG  
AGCTGGCTAGCATCCTCTAGGGCCCCGCCACGTTGCCCGAAGCCACCATGCAGAAGGCCACAG  
AAGGGATCAGGACCTGTCTGCCGGCTTGTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA  
CTGAAGACTCAAGGAGGTGGCCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG  
TGGCCTCCTGCCTCCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA  
TGCCAAGGACTGATCGGGCCTAGCCCGGAACACTAATGTAGAAACCTTTTTTTTACAGAGCC  
TAATTAATAACTTAATGACTGTGTACATAGCAATGTGTGTGTATGTATATGTCTGTGAGCTA  
TTAATGTTATTAATTTTCATAAAAGCTGGAAAGC

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**FIGURE 12**

MWLRWALS LPPSSCLWAEPGMPSQTPWWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG  
SCPTSHTARPIGT CFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL  
GTAIQGQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV  
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPIYIKLITGFLFTSLAFMLVEGNFVLFCT  
YTLGFRNEFQNL LLAIMLSATLTIPIWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI  
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG  
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKKAL  
QALRDEASSSGCSETDSTELASIL

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**FIGURE 13**

GGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT  
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTGA  
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACCTTA  
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACCTTGTCTTGTTT  
TGCACCTACACCTTGGGCTTCCGCAATGAATTCAGAATCTACTCCTGGCCATCATGCTCTC  
GGCCACTTTAACCATTCCCATCTGGCAGTGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG  
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAAC  
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT  
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG  
GAACCGAGCCCCAT

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**FIGURE 14**

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT  
ATGAGCAGGTCTGAAGACTAACATTTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGT  
GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT  
TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT  
CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG  
CAGTTTTATGCATTGCTACCATTTATGTTCTGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA  
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTAAGTGGGCAATGCTAAATATTGCGG  
ACTTTCTATTGTGGCAAACCTCCAGAAAACAACCCCTTTTTGCTGCACATGTAAGTGGAGCTG  
TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCTACCAAATG  
CAGCCCCAAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG  
AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG  
ATTTAGAACAGAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT  
ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTTGGTTTTTTCCTGACTTACATTCGTGA  
TTTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCCTCTATGACACTG  
CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCCAGAGATATTTGATGAAAGGAT  
AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTACAGAAAGTTGCTTA  
TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA  
ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA  
TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAGACTATG

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**FIGURE 15**

MWWFQQGLSFLPSALVIWTSAAFIIFS YITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI  
AAVLCIATIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG  
AVLTFGMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG  
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLT YIRDFQKISLRVEANLHGLTLYD  
TAPCPINNERTRLLSRDI

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**FIGURE 16**

CGGACGCTTGGGCNGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCTGATGCCGAGT  
TCCGTCTCTCGGGTCTTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA  
GTGCTTCGCGCTTCCGGAGAAAATCAGCGGTCTAATTAATTCCTCTGGTTTGTGGAAGCAGT  
TACCAAGAATCTTCAACCCTTCCCACAAAAGCTAATTGAGTACACGTTCTGTTGAGTACA  
CGTTCCTGTTGATTTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTTTGTGAA  
GTTGTAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCT  
TCAGCCCTTGTAATTTGGACATCTGCTGCTTTCATATTTTCATACATTACTGCAGTAACACT  
CCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGGTACAGTANC

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**FIGURE 17**

CCCACGCGTCCGCCCCGCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGGG  
CCGGGGTGCGGAGCCGACATGCGCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC  
CTTCGCCTTGCTACTTGCTGTGCGACGCGACTGCCCCGCGGGCGGAGACTGGGCTCCACCGAGG  
AGGCTGGAGGCAGGTCGCTGTGGTTCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG  
GTCCCTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCTGCTCTTCTGCGGCGCCTA  
CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCCTGAATGTTTTAGCTGGTGCCT  
TGTTTGGGCCATGGCTGGGGCTTCTGCTGTGCTGTGTGTTGACCTCGGTGGGTGCCACATGC  
TGCTACCTGCTCTCCAGTATTTTTGGCAAACAGTTGGTGGTGTCTACTTTCCTGATAAAGT  
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAACAGAAACAGCTTGTTTTTTTTCTTATTGTTTT  
TGAGACTTTTCCCCATGACACCAAACCTGGTTCTTGAACCTCTCGGCCCAATTCTGAACATT  
CCCATCGTGCAAGTTCTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTTTCATCTGTGT  
GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGGACACTG  
TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAAATCCTGGAACCCTCATTAAAAAATTT  
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACACAGTAGAAAAGA  
CACATGATGATCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA  
TGTGGTCTCTAAAGCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG  
CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT  
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT  
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATTC  
ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAAT  
ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC  
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT  
CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC



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**FIGURE 18**

MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR  
KEHQAYVFLFLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSVGATCCYLLSS  
IFGKQLVVSYPDPKVALLRKVEENRNSLFFFLFLRLFPMTPNWFLNLSAPILNIPIVQFF  
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKSQKHLQ  
LNETSTANHIHSRKDT

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domains:**

amino acids 101-123, 189-211

**N-glycosylation sites.**

amino acids 172-176, 250-254

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 240-244, 261-265

**N-myristoylation site.**

amino acids 13-19, 104-110, 115-121, 204-210

**Amidation site.**

amino acids 27-31

**Prokaryotic membrane lipoprotein lipid attachment site.**

amino acids 4-15

**Protein splicing proteins.**

amino acids 25-31

**Sugar transport proteins.**

amino acids 162-172

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**FIGURE 19**

CCGAGGCGGGAGGAGCCCGAGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATTTT  
CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA  
TAGGAAAATAACTTGGGATTTTATATTGGAAGACATGGATCTTGCTGCCAACGAGATCAGCA  
TTTATGACAACTTTTCAGAGACTGTTGATTTGGTGAGACAGACCGGCCATCAGTGTGGCATG  
TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC  
CCCCCGCAGTATCCTCTCCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT  
TGCTCACTGCCTACTTTGTGATTCAACCTTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTCT  
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA  
GAAGTACATGTCAGAAAATAAGGGAGTTCTCTGCATGGGGGTGATGAAGACAGACCCTTTTC  
CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTCTGCC  
AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA  
ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCCTGTTGGAGGAAGAGATTC  
AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG  
TGGTGGCGCTGCTTTCTTGAGCGGTGGTTCCCATTCTCTTATCCATGGAGGAGACCTCTGAA  
CAGATCACAAATGTTACGTGAGCTTTTTCTGTGTTTCACTCACCTGCCATTTCCAAAAGATG  
CCTCTTTAAACAAGTGCTCCTTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG  
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTTCCA  
GTGCCGAAGACATTGTCACTGTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTCTG  
ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT  
GGAACCGCTTTCTCAGAACTGTAGGAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA  
AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAACGATGAAACTGCAAAA

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**FIGURE 20**

MDLAANEISIIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY  
KVLATLGLILLTAYFVIQPFSPLAPEPVLPGAHTWRSLIHHIRLMSLPIAKKYMSENKGVPL  
HGGDEDRPFPDFDPWWTNDCEQNESEPIPANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT  
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPPYPWRRPLNRSQMLRELFV  
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRHCSVAMP  
IEPGDIGYVDTHWKVYVIARGVQPLVICDGTAFSEL

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**FIGURE 21**

CCACGGTGTCGGTTCTTCGCCCCGGCGGCAGCTGTCCCCGAGGCGGGAGGAGCCCCGAGGGGCG  
CGAGCCCCGCATGAATCATTGTAGTCAATCATTTTCCAGTTCTCAGCCGTTTCAGTTGTGATC  
AAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAATAGGAAAATAACTTGGGATTTTATATT  
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTTATGACAACTTTCAGAGACTGTTG  
ATTTGGTGAGACAGACCGGCCATCAGTGTGGCATGTCAGAGAAGGCAATTGAAAAATTTATC  
AGACAGCTGCTGGAAAAGAATGAACCTCAGAGACCCCCCGCAGTATCCTCTCCTTATAGT  
TGTGTATAAGGTTCTCGCAACCTTGGGATTAATCTTGCTCACTGCCTACTTTGTGATTCAAC  
CTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTGTGGAGCTCAC

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**FIGURE 22**

CCCACGCGTCCGCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG  
CAGGGTCCCCACTTGCAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG  
CCACTGGTGCGCACGCTGCTAGACCGTGCCTATGAGCCGCTGGGGCTGCGAGTGGGACTGCC  
CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA  
CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACCA**ATGT**CCAGTTCGAAATG  
GACACGTATGCTAAGAGCCACGACCTTATGTCAGGTTTCTGGAATGCCTGCTATGACATGCT  
TATGAGCAGTGGGCAGCGCGCCAGTGGGAGCGCGCCAGAGTCGTCGGGCCTTCCAGGAGC  
TGGTGCTGGAACCTGCGCAGAGGCGGGCGCGCCTGGAGGGGCTACGCTACACGGCAGTGCTG  
AAGCAGCAGGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGCGCTGTGGCGCCAGCT  
CGCCAGCCCATGTGGGGCCTGGGGCGCTGAGGGACACTCCCATCCCCCGCTGGAAACTGTCCA  
GCGCCGAGACATATTACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC  
CTGGAAGCCAGCGCTCTCCGAGACAATCTGGGTGAGGTTCCCCTGACACCCACCGAGGAGGC  
CTCACTGCCTCTGGCAGTGACCAAGAGGCCAAAGTGAGCAGCCCAACCCAGGTTGCTGCGAGG  
AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCCGATGGAGGCAGCAGAACTG  
GATGAGCAGCGTGAGAAGCTGGTGCTGTCGGCCGAGTGCCAGCTGGTGACGGTAGTGCCCGT  
GGTCCCAGGGCTGCTGGAGGTCACCACACAGAATGTATACTTCTACGATGGCAGCACTGAGC  
GCGTGGAAACCGAGGAGGCATCGGCTATGATTTCCGGCGCCCACTGGCCCACTGCGTGAG  
GTCCACCTGCGGCGTTTCAACCTGCGCCGTTTACGCACTTGAGCTCTTCTTTATCGATCAGGC  
CAACTACTTCCCTCAACTTCCCATGCAAGGTGGGCACGACCCAGTCTCATCTCCTAGCCAGA  
CTCCGAGACCCAGCCTGGCCCCATCCCAACCCATACCCAGGTACGGAACCAAGGTGACTCG  
TGGCTCCTGCGCCTACGGCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT  
GCTGCGTGCCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACCTTCGAGTACT  
TGATGCAACTCAACACCATTTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTC  
CCCTGGGTCTGTCAGGACTACGTGTCCCAACCCCTGGACCTCAGCAACCCAGCCGTCTTCCG  
GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCAGCTCGTGAGGGAGAAGT  
ATGAAAGCTTTGAGGACCCAGCAGGGACCTTGACAAGTTCCACTATGGCACCCCACTACTCC  
AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGGAGCCCTTACCTCCCTGCACGTCCA  
GCTGCAAAGTGGCCGCTTTGACTGCTCCGACCGGCAGTTCCACTCGGTGGCGGCAGCCTGGC  
AGGCACGCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCTCT  
GACTTCCCTGGAGAACCAGAACGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT  
AGGCGATGTGGTGCTACCCCCGTGGGCCAGCTCTCCTGAGGACTTCATCCAGCAGCAGCGCC  
AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC  
TACAAGCAGCGGGGGCCAGCCGCGGAGGAGGCCCTCAATGTCTTCTATTACTGCACCTATGA  
GGGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATT  
TCAGCAACTTTTGGGACAGCTCCCTGTGAGCTGTGAAGGAGCCACATCCAACCTCGGCTCTCA  
GCTGAGGAAGCAGCCCATCGCCTTGACGCGCTGGACACTAACTCACCTAGCATCTTCCAGCA  
CCTGGACGAACCTCAAGGCATTCTTCCGAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA  
CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAAGACCCC  
ACCATGGGCAGCCACAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT  
GAGTGGACAAGCACTGGCAGTGGCCCCGGATGGAAAGCTGCTATTTCAGCGGTGGCCACTGGG  
ATGGCAGCCTGCGGGTGAAGTGCACCTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTGCCAC  
CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG  
GGACACCAGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTGAGTAGGCTGGCAC  
CAAAGCCTGTGCAGGTCCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT  
GAACTTGACATGGCTGTGTCTGGATCTGAGGATGGAAGTGTGATCATAACACTGTACGCCG  
CGGACAGTTTTGTAGCGGCACTACGGCCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC  
TGGCATTTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCCTGGGGCC  
CAGGTCACCTACTCCTTGACCTGTATTTCAGTCAATGGGAAGTTGCGGGCTTCACTGCCCT  
GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCAGT  
GCGCCCTGCACATCCTCCAACCTAAACACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG  
GTGGCCATCCGCAGCGTGGCCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCCTGGAGGA  
TGGCAAGCTCATCGTGGTGGTTCGCGGGGCGAGCCCTCTGAGGTGCGCAGCAGCCAGTTTCGCG  
GGAAGCTGTGCGGCTCCTCGCGCGCATCTCCAGGTGTCTCCTCGGGAGAGACGGAATACAAC  
CCTACTGAGGCGCGCT**TGA**ACCTGGCCAGTCCGGCTGCTCGGGCCCCGCCCCGGCAGGCCTG  
GCCCCGGAGGGCCCCGCCAGAAGTCGGCGGGAACACCCCGGGTGGGCAGCCAGGGGGTGA  
GCGGGGCCACCCCTGCCAGCTCAGGGATTGGCGGGCGATGTTACCCCTCAGGGATTGGCG  
GGCGGAAGTCCCGCCCCCTCGCCGGCTGAGGGGCCGCCCTGAGGGCCAGCACTGGCGTCT

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**FIGURE 23**

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL  
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN  
HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELALEETP  
MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETEEGIGYDFRRP  
LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTTPVSSPSQTPRPQPGPIPPHTQV  
RNQVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRTYNDL  
SQYPVFPWVLQDYVSPTLDLSNPAVFRDLSKPIGVVNPKHAQLVREKYESFEDPAGTIDKFH  
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDRQFHSVAAAWQARLESPADVKELIP  
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPPWASSPEDFIQQHRQALESEYVSAHLHEW  
IDLIFGYKQRGPAEEEEALNVFYCYCTYEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP  
HPTRLSAEEAAHRLARLDTNSPSIFQHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF  
SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWGDSLRTALPRGKLL  
SQLSCHLDVVTCLALDTCGIYILISGRDTCMVWRLLHQGGLSVGLAPKPVQVLYGHGAAS  
CVAISTELDMAVSGSEDGTVIIHTVRRGQFVAALRPLGATFPGPFIHFLALGSEGQIVVQSSA  
WERPGAQVTYSLHLYSVNGKLRLASLPLAEQPTALTVTEDFVLLGTAQCALHILQLNTLLPAA  
PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVVAGQPSEVRSSQFARKLWRSSRRISQVSS  
GETEYNPTEAR

**N-glycosylation site.**

amino acids 677-681

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 985-989

**Tyrosine kinase phosphorylation site.**

amino acids 56-65, 367-376, 543-551

**N-myristoylation site.**amino acids 61-67, 436-442, 604-610, 610-616, 664-670, 691-697,  
706-712, 711-717, 769-775, 785-791, 802-808, 820-826, 834-840,  
873-879, 912-918, 954-960

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**FIGURE 24**

CGGACGCGTGGGCGGACGCGTGGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCC  
CACGGCCACCTTGTGAACTCCTCGTGCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT  
CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGGGCTCTTC  
TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT  
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC  
GCACACTCCGTTACCACACTGGGTCAATTGGCATTGGAGCCCTCATCCTGACCCTTGTGCAG  
ATAGCCCGGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCTGTAGC  
CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC  
TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA  
AATGCGTTCATGCTACTCATGCGAAACATTGTGAGGGTGGTCTGCTGGACAAAGTCACAGA  
CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTCTGGAGGCGTGGGGGTCCTGTCCTTCTTTT  
TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCACCTCAACTATTAC  
TGGCTGCCCATCATGACCTCCATCCTGGGGGCCTATGTCATCGCCAGCGGCTTCTTCAGCGT  
TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG  
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC  
GAGGCGCCCCCGGACAACAAGAAGAGGAAGAAGTGAACAGCTCCGGCCCTGATCCAGGACTGC  
ACCCACCCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT  
AAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG  
AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC  
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCATCCCAGCTAC  
TCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCGGGAGGCAGAGGTTGCAGTGAGCCGAGA  
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAAACAA  
AAAGATTTTATTAAAGATATTTTGTAACTC

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**FIGURE 25**

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVGLGF  
WTLNWWLALGQCVLGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQ  
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK  
NAFMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY  
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLLKILGKN  
EAPPDNKKRKK



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**FIGURE 26**

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT  
GGCTATGTTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC  
TTCTCTTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTTC  
CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGC  
ATTTCTTGAGCATAAAGAACAGTTTCATTATTTTATTCTCATAACTGTGGAGCTAATGTAG  
ACCTATTGGATATTCTTCAACCTGATGAAGACACTATATTCTTTGTGTGTGACTCCCATAGG  
CCAGTCAATGTGTCGTCATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA  
TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT  
CAGGAAATGACAGTGATGGGTGAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA  
GTGGAGCAAACCATGCGGAGGAGGCAGCGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT  
CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG  
CTTGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC  
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCTTGCAGCG  
CCACGTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA  
CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC  
AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA  
GCGGCTCCAGGAGTTCCTTGACAGATGGGTCTTCCCTGAAGCAGGTGAAGCAGAAAGTTCC  
AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA  
TTTGGGATGAAGGACATGCGCGTGCAGACTTTCAGCATTCATTTTGGGTCAAGCACAAGTT  
TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT  
CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG  
TACCATGGCCTGGAACCTCGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC  
CTTTGCACCAACCTCGTCATCTCCAGGGGCCTTTCTGTACTGCTCTCTCATGGAGGGCAC  
TCCAGATGTCATGCTGTTCTCTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA  
AGTCCTTTGTGTGTTGACAAAGAACCGGCGCTGCAAACCTGCTGCCCTGGTGATGGCTGCC  
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCAGAGACCGACAGCTC  
GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA  
TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT  
CTGGACGCACTTATTTCCCTCCTGTCCTAGGAATTTGATTCTTCCAGAATGACCTTCTTATT  
TATGTAACCTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT  
TTTTATTAAATAAAATGCTTATTTTAGGAAA

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**FIGURE 27**

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF  
LEHKEQFHYFILINCGANVDLLDILQPDEDTIFVCDSHRPVNVVNVYNDTQIKLLIKQDDD  
LEVPAIEDIFRDEEEDEEHSGNDSGSEPSEKRTRLEEEIVEQTMRRRQRREWEARRRDILF  
DYEQYEHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLRH  
VSRHNRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSL CNTSYTAARFKLWSVHGQKR  
LQEFLADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTF SIHFGFKHKFL  
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLRSNLDKLYHGLELAKKQLRATQQTIASCL  
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP  
LSMEHGTVTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHFDLSVIELKAEDRSKFL  
DALISLLS

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**FIGURE 28**

GTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCGCTGGCTATGNTCGTGTCCGATTTCCGCA  
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCCTTCTCTTCGTGGCCTCGGANGTGGAT  
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGACCANGTGCAATATANGCT  
GGTTCAGTTTCTGGGTGGCAAGAACTTGAACTGCATTTCTTGAGCATAAAGAACAGTTTC  
ATTATTTTATTCTCATAAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT  
GAAGACACTATATTCTTTGTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA  
CGATACCC

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**FIGURE 29**

CAGGAACCCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC  
CACGAAGGGGACGATACCAGAAAAACACCCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG  
GCTGACTTTTGGCTATAGAAAAAAGAAAGAACGAAAAGAGACAGTTTTTTTTTGGAAAGCTAA  
GTCTTCCCTTTATCGAGTCAAGAAACCCCCCTTCTTGAGCTATTTACAGCTTTTAAACAATT  
GAGTAAAGTACGCTCCGGTCACCATGGTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC  
CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC  
CAGCGGCTGCCAACGGTGTGTGACTCTGAGGACCCCTGGATCCTGCCCATGTATCCTCAG  
CCTCTTCCCTCCGGCCGCCCCACGCCCTGCCCTGAGATCAGACCCTACATTAATATCACCATC  
CTGAAGGGTGACAAAGGGGACCCAGGCCCAATGGGCCTGCCAGGTACATGGGCAGGGAGGG  
TCCCCAAGGGGAGCCTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGGAGATGGGCAGCCCCG  
GCGCCCCGTGCCAGAAGCGCTTCTTCGCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC  
GGCAGGACTTCCAGACGCTGCTCTTCGAAAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA  
CATGGCGACCGGCCAGTTTGTGCTCCCCCTGCGTGGCATCTACTTCTCAGCCTCAATGTGC  
ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTATC  
CTGTACGCGCAGCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC  
CTACGGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCGAGAACGCCATCTACAGCA  
ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGACTGAGGGG  
CCTCTGGGCCACCCCTCCCGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTGCAGGGCTCAG  
TTTGCCTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCCGGGGACCTGGCATTCTGGGGAGA  
CCCTGCTTCTATCTTGGCTGCCATCATCCCTCCCAGCCTATTTCTGCTCCTCTCTTCTCTCT  
TGGACCTATTTAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCCAGCCTCGTAGCCC  
AGCACTTCTCAAACCTTGGAAATGCATGCGAATCACCCGGGGTTCGTGTTAAATGCAGATTCT  
GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCCCTGGGTGATGCTG  
ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG  
TACTTTCTGAACATTCTGGAATCCTCCCCACATTCTAGAACTTCTCCCAACATTTTTTTTTTCT  
TGAGACAGAGTCTTGCTCTGTTGCCAGGCTAGAGTGCAGTGGTGCATCTCAGTTCACTGC  
AACCTCTGCCTCCCGGGTTCAAGCGATTCTTGCTCAGCCTCCCTAGTGGCTGGGATTAC  
AGGCGCCTGCTACCATGCCTGGCTAATTTTTGTATTTTAGTAGAGATGGGGTTTCACCATA  
TTGGCCAGGCTGGTCTTGAACCTCCTGACTTCAGGTGACCCACCCGCTCGGCCTCTCAAAT  
GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT  
CCCTCCAGGGCTCCCGTGCTATGTTCTCTTACCCCTTCCCCCTCTTCTCTTGCTCAGGCC  
TGCACCACTGCAGCCACCGTTCATTTATTTCATTATTAACACTGAGCACTCACTCTGTGCT  
GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGAAGTGGCCA  
GTCCAGCCCAGGCGGGGAGAGATGTGTACATAGGTTTTAAAGCAGACCCAGAGCTCATGGGG  
GCCTGTGTTCTGGGTGTTTCAGGTGCTGCTGGTCCCTCCATTACCCACTGCTCCCCAAGGCTGG  
TGGGACGGGGTCCCGGTGGCAGGGGCAGGTATCTCCTTCCCGTTCCCTCATCCACCTGCCAG  
TGCTCATCGTTACAGCAAAACCCAGGGGGCTTGGCCAGGTCAAGGGTCTGTGAGGAGAGG  
ACCCAGGAGTGTGGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA  
TAGCTCTCCCCACAGCTGATACGGCATCCTGCGAGAAGACCTGCCCTCCTCACTGGGATCCC  
CTTCTGCCTCCTCCCAGGGCTCTGCCAGGGCCTTGTCTCAGTCCCTTCCACCAAAGTCATCT  
GAACTTCCGTTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGTCCCCAGGTGCT  
CTCTGCCCCCTCATGCCCCCTCTCACCGGCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG  
CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGTGCTTCTTAC  
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG  
AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTTCTTCTCCAGGGTGGGGTGGCCTGGT  
GTTCCCTTAGCCTTCCAAACCCAGGTGGCCTGCCCTTCTCCCAGAGGGAGGCGGCCTCCGC  
CCATTGGTGTCTATGCAGACTCTGGGGCTGAGGTGCCCCGGGGGTGATCTCTGGTGTCTCAC  
AGCCGAGGGAGCCGTGGCTCCATGGCCAGTACGCGAAACAGGGTCTGACCAAGTGCCAGGA  
AGACCTGTGCTATAAACACCCCTGCCTGATCTGCCCCCTGCCTGACCCCGCACGCCCTGCC  
GTCCAGCATGATTAAAGAATGCTGTCTCTCTTGGAAAAA

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**FIGURE 30**

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSSGRPH  
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEFPGPQGSKGDKGEMGSPGAPCQKRF  
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET  
YVHIMHNQKEAVILYAQPSESRIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT  
FSGHLIKAEDD

**Important features:**

**Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 72-75

**Clq domain proteins.**

amino acids 144-178, 78-111 and 84-117

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**FIGURE 31**

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCCGACCCGCCAGGAAAGACTG  
AGGCCGCGGCCTGCCCCGCCCCGGCTCCCTGCGCCGCCGCCCTCCCGGGACAGAAG**ATGTG**  
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG  
GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG  
ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT  
CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGCTCCTGGACCTGTCAC  
AGAACCAGATCGCCAGCCTGCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG  
GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT  
CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC  
TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCCGCTGCGC  
CTGCCCCGCCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCCGGCAT  
CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACG  
AGGGGCTCTTCAGCCGCTTGCGCAACCTCCACGACCTGGATGTGTCCGACAACAGCTGGAG  
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACAC  
CCGATTGCCAGCTGCGGCCCCGAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATG  
TGAGCAACCTAAGCCTGCAGGCCCTGCCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG  
CTGCTGGCAGCTGCCCGCAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCCTG  
GGTGCGCGAGAGCCACGTCACTTGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCCGCCCA  
AGAAGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCCAGCCACCACC  
ACCACAGCCACAGTGCCACACGAGGCCCCGTGGTGCGGGAGCCCACAGCCTTGTCTTCTAG  
CTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGGCCACTGAGGCCCCCAGCCCCGCCCTCCA  
CTGCCCCACCGACTGTAGGGCCTGTCCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTC  
AATGGGGGCACATGCCACCTGGGGACACGGCACCACTGGCGTGCTTGTGCCCCGAAGGCTT  
CACGGGCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCCAGCCCTACACCACTCA  
CGCCGAGGCCACACGGTCCCTGACCCCTGGGCATCGAGCCGGTGAGCCCCACCTCCCTCGCG  
GTGGGGCTGCAGCGCTACCTCCAGGGAGCTCCGTGCAGCTCAGGAGCCTCCGTCTCACCTA  
TCGCAACCTATCGGGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTG  
AGTACACGGTCACCCAGCTGCGGGCCCAACGCCACTTACTCCGTCTGTGTGATGCCTTTGGGG  
CCCCGGCGGGTGCCGGAGGGCGAGGAGGCCTGCGGGGAGGCCCATACACCCCCAGCCGTCCA  
CTCCAACCACGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCCCG  
CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGCAGCCTACTGTGTGCGGCGG  
GGGCGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCTT  
GGAAGTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG  
AGGCCCTGCCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCAGGGCCTGGCCTC  
CAGTCACCCCTCCACGCAAAGCCCTACATC**TAA**GCCAGAGAGAGACAGGGCAGCTGGGGCCG  
GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC  
CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA  
CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCCAGCTGACGAGCCCTAACGTCCCCAGAAC  
CGAGTGCCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG  
GGCCTGCCATGTGCTGGTAACGCATGCCTGGGTCTGCTGGGCTCTCCCACTCCAGGCGGA  
CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG  
TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAGAACTGGAAAGGAAGATGCTTTA  
GGAACATGTTTTGCTTTTTTAAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG  
GGAAGATGTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTTGTAAGACAAACGATGATATG  
AAGGCCTTTTGTAAGAAAAAATAAAAGATGAAGTGTGAAA

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**FIGURE 32**

MCSRVP LLLPL LLL LALGPGVQGCPSGCQCSQPQT V FCTARQGTTVPRDVPPDTVGLYVFEN  
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR  
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRL LLLDLSHNSLLALEP  
GILDTANVEALRLAGLGLQQLDEGLFSRLRNLDLDVSDNQLERVPPVIRGLRGLTRLRLAG  
NTRIAQLRPEDLAGLAALQELDVSNSLQALPGDLSGLFPRLRLAAARNPFNCVCPLSWFG  
PWVRESHVTLASPEETRCHFPK NAGRLLELDYADFGCPATTTTATVPTTRPVVREPTALS  
SSLAPT WLSPTAPATEAPSPPSTAPPTVGPVPQPQDCPPSTCLNGGTCHLGRHHLACLCPE  
GFTGLYCESQMGQGTRPSPTPVTPRPPRSLTGIEPVSPTS LRVGLQRYLQGSSVQLRSLRL  
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA  
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPAG  
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGPGLQSPLHAKPYI

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**FIGURE 33**

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGCAAGCCGTGGGGGTTTTGAGCTCAT  
CTTCATCATTCATATGAGGAAATAAGTGGTAAATCCTTGGAAATACAATGAGACTCATCAG  
AAACATTTACATATTTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG  
AAGAAAGGGAACTGATGACCAACTGCTCCAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG  
ACCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTTCA  
TTTTCATTTCTGTCTCCAAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG  
ATCTCAAAACCTTTGAATTCACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG  
AAGAGTGTAACTTGGTATTTACTGGCAGGTCTCAGGTATTTAGATCTTTCTTTTAAATGACTT  
TGACACCATGCCTATCTGTGAGGAAGCTGGCAACATGTCACACCTGGAAATCCTAGGTTTGA  
GTGGGGCAAAAATACAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC  
TTCTTAGGATTCAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC  
AAAATGACATTTGTTTACCAATGGACACAATTTCTGGGTTCTTTTGGCTGATGGAATCA  
AGACTTCAAAAATATTAGAAATGACAAAATATAGATGGCAAAAGCCAATTTGTAAAGTTATGAA  
ATGCAACGAAATCTTAGTTTGAAGAAATGCTAAGACATCGGTTCTATTGCTTAAATAAGTTGA  
TTTACTCTGGGACGACCTTTTCTTATCTTACAATTTGTTTGGCATAACATCAGTGGAACT  
TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCATTTGACTAC  
TCAAATACTGTAATGAGAACTATAAAATTTGGAGCATGTACATTTAGAGTGTTTTACATTTCA  
ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG  
CACAAATGCCACACATGCTTTTCCGAATTATCCTACGAAATTCGAATATTTAAATTTTGCC  
AATAATATCTTAACAGACGAGTTGTTTAAAGAAGCTATCCAAGTGCCTCACTTGAAAACCTCT  
CATTTTGAATGGCAATAAACTGGAGACACTTTCTTTAGTAAGTTGCTTTGCTAACAACACAC  
CCTTGGAAACCTTGGATCTGAGTCAAAATCTATTACAACATAAAAAATGATGAAAATTGCTCA  
TGGCCAGAACTGTGGTCAATATGAATCTGTCATAACAATAAATTGTCTGATTCTGTCTTCAG  
GTGCTTGGCCAAAAGTATTCAAATACTTGACCTAAATAATAACCAATCCAACTGTACCTA  
AAGAGACTATTCATCTGATGGCCTTACGAGAATAAATATTGCATTTAATTTTCTAAGTAT  
CTCCCTGGATGCGAGTCATTTTCTAGTAGACTTTTCTGATTCTGAACATTGAAATGAATTCATTT  
CAGCCCATCTCTGGATTTTGTTCAGAGCTGCCAGGAAGTTAAACTCTAAATGCGGGAAGAA  
ATCCATTCCGGTGTACCTGTGAATTAATAAATTTTCTATTGAAACATATTTCAGAGGTC  
ATGATGGTTGGATGGTCAGATTCATACACCTGTGAATACCCTTTAAACCTAAGGGGAAGTAG  
GTAAGAGAGCTTTCATCTCCACGAATTATCTTGCAACACAGCTCTGTTGATTGTACCATTTG  
TGGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC  
TGGTATCTCAGGATGCTAGGTCAATGCACACAACATGGCACAGGGTTAGGAAAACAACCCA  
AGAACAACCTCAAGAGAAATGTCCGATTCCACGCATTTATTTTCATACAGTGAACATGATTCTC  
TGTGGGTGAAGAATGAATTGATCCCCAATCTAGAGAAGGAAGATGGTTCTATCTTGATTGTC  
CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCAATTGA  
GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCAACTTTGTCCAGAATGAGTGGTGCCATT  
ATGAATTCTACTTTGCCCACCACAATCTCTTCCATGAAAATTCTGATCATATAATTCTTATC  
TTACTGGAACCCATTCCATTCTATTGCATTTCCACCAGGTATCATAACTGAAAGCTCTCCT  
GGAAAAAAGCATACTTTGGAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA  
ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA  
TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT  
ATAAATCCACAGTCTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA  
CAACCTTTATGATGGCAATTTGACAATATTTATTAATAAATAAATAAGTTATTTCCCTTCATA  
TCAGTTTCTAGAAGGATTTCTAAGAATGTATCCTATAGAAACACCTTCACAAGTTTATAAGG  
GCTTATGAAAAAGGTGTTTCATCCCAGGATTGTTTATAATCATGAAAAATGTGGCCAGGTGC  
AGTGGCTCACTCTTGTAAATCCCAGCACTATGGGAGGCCAAGGTGGGTGACCCACGAGGTCAA  
GAGATGGAGACCATCCTGGCCAACATGGTGAAACCTGTCTCTACTAAAAATACAAAAATTA  
GCTGGGCGTGATGGTGCACGCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCG  
CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCCTCCAGCCTGGT  
GACAGAGCGAGACTCCATCTCAAAAAAAGAAAAAAGAAAAAATGGAAAACATCC  
TCATGGCCACAAAATAAGGTCTAATTCAATAAATTATAGTACATTAATGTAATATAATATTA  
CATGCCACTAAAAAGAATAAGGTAGCTGTATTTTCTGGTATGGAAAAACATATTAATAT  
GTTATAAATCTTAGGTTGGTGCAAACTAATGTGGTTTTTGGCATTGAAATGGCATTGAA  
ATAAAGTGTAAGAATCTATACCAGATGTAGTAACAGTGGTTTTGGGTCTGGGAGTTGGA  
TTACAGGGAGCATTTGATTTCTATGTTGTGTATTTCTATAATGTTTGAATTGTTTAGAATGA  
ATCTGTATTTCTTTTATAAGTAGAAAAAATAAAGATAGTTTTTACAGCCT



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**FIGURE 34**

MRLIRNIYIFCSIVMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ  
LQSSDFHVSVKLRVLILCHNRIQQDLKTFFFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL  
SFNDFDTPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP  
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL  
LNKVDLLWDDFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR  
VFYIQQDKIYLLLTkMDIENLTISNAQMPHMLFPNYPTKFQYLNfANNILTDELfKRTIQLP  
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSQNLLQHKNdENCsWPETVVNMNLSYNKLS  
DSVFRCLPKSIQILDNLNNQIQTVPKETIHLMALRELNIAFNFLTDLPGCshFSRLSVLNIE  
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN  
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVGLAVAFCClHFDLPWYLRMLGQCTQTWHRV  
RKTtQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI  
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHhNLFHENSdHIILILLEPIPFYCIPTRYHK  
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM  
RTDCL

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**FIGURE 35**

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGTGCGCGGGAAAGG  
GAGGGAAGAAGGAAGGGCGGGCCGGCCCCCTGCGCCCCCGCGCCTCTGCGCGCCCTGTCCGCCCCGGC  
CCAGCCAGCCCCAGCCCCGCGGGCCGGTCAACACGCGAGCCAGCCGGCCGCTCCCGGCCCAAGCGCCCGCT  
CTGCTGTGCCCTGCGCCCTTGCCCCGCGCCAGCTTCTGCGCCCGAGCCCGCCCGCGCCCCGGTGACCGTGA  
CCCTGCCCTGGGCGCGGGGCGGAGCAGGCATGTCCTCCCGCCGGGACCGCTACCCAGCGCTGGCCCTGGTGCTC  
CTGGCAGTGACCTGGCCGGGGTCTGGAGCCAGGGCGCAGCCCTCGAGGACCCTGATTATTACGGGCAGGAGAT  
CTGGAGCCGGGAGCCCTACTACGCGCGCCCGGAGCCCGAGCTCGAGACCTTCTCTCCGCGCTGCTGCGGGC  
CCGGGAGGAGTGGGAGCGCGCCCGCAGGAGCCAGGCCGCCAAGAGGGCCACCAAGCCCCAAGAAAGCTCCC  
AAGAGGGAGAAGTCGGCTCCGGAGCCGCTCCACAGGTAAACACAGCAACAAAAAGTTATGAGAACCAGAG  
CTCTGAGAAGGCTGCCAACGATGATCACAGTGTCCGTGTGGCCCGTGAAGATGTGAGAGAGATTGCCACCTC  
TTGGTCTGGAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCCTGGGGCA  
CATCGAGGGAGACTCAACATCCAGGCGGGCATTAAATGAAATGATTTTTATGACGGAGCGTGGTGCGCGGGAAG  
AAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCTGACCAGATTCACTGGTGTCATCACTCAAGGGA  
GGAATCCCTCTGGCTGAGTGACTGGGTGACATCCTATAAGGTGATGGTGAGCAATGACAGCCACACGTGGGCT  
ACTGTTAAGAATGGATCTGGAGACATGATATTTGAGGGAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCT  
ACCCGTCCCATGGTGGCCCGTACATCCGCATAAACCTCAGTCTGTTGATAATGGGAGCATCTGCATGA  
GAATGGAGATCCTGGGCTGCCACTGCCAGATCCTAATAATTATTATCACCGCCGGAACGAGATGACCACCT  
GATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCAGTTGATGAAAGTTGTGAATGAAATGTGTCC  
CAATATCACAGAATTTACAACATTGGAAAAAGCCACAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATC  
ACCCTGGGAGCATGAAGTCGGTGAGCCCGAGTTCCACTACATCGCGGGGGCCACGGCAATGAGGTGCTGGGC  
CGGGAGCTGCTGCTGCTGCTGGTGCAATTCTGTGTGTCAGGAGTACTTGGCCCGGAATGCGCGCATCGTCCACCT  
GGTGGAGGAGACGCGGATTACGTCTCTCCCTCCCTCAACCCCGATGGCTACGAGAAGGCCTACGAAGGGGCT  
CGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCAGATGGAATTGACATCAACAACAACCTTCTGATTTA  
AACACGCTGCTCTGGGAGGCGAGGATCGACAGAATGTCCCGAGGAAAGTTCCCAATCACTATATTGCAATCCC  
TGAGTGGTTTCTGTGCGAAAATGCCACGGTGGCTGCCGAGACCAGAGCAGTCAATAGCTGGATGGAAAAAATCC  
CTTTTGTGCTGGGCGGAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCCC  
TGGAAGACGCGAGGAACACACCCCCACCCCGATGACCACGTGTTCCGCTGGCTGGCCTACTCCTATGCTCCAC  
ACACCGCTCATGACAGACGCCCCGAGGAGGGTGTGCCACACGGAGGACTTCCAGAAGGAGGAGGGCACTGTCA  
ATGGGGCCTCTGGGACACCCGTGCTGGAAGTCTGAACGATTTACGCTACCTTCATACAACTGCTTCGAAGT  
TCCATCTACGTGGGCTGTGATAAATACCCACATGAGAGCCAGCTGCCGAGGAGTGGGAGAATAACCGGGAATC  
TCTGATCGTGTTCATGGAGCAGGTTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTACATGGAAAAGGAATCC  
CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGATTACTGGCGCCTC  
CTGAACCTGGAGAGTATGTGGTCAACAGCAAAGGCCGAAGGTTTCACTGCATCCACCAAGAACTGTATGGTTGG  
CTATGACATGGGGGCCACAAGGTGTGACTTCACACTTAGCAAAACCAACATGGCCAGGATCCGAGAGATCATGG  
AGAAGTTTGGGAAGCAGCCCGTCAGCCTGCCAGCCAGCGGCTGAAGCTGCGGGGGCGGAAGAGACGACAGCGT  
GGGTGACCCCTCTGGGCCCTTGAGACTCGTCTGGGACCCATGCAAATTAACCAACCTGGTAGTAGCTCCATAG  
TGGACTCACTCACTGTTGTTTCTCTGTAATTCAGAAGTGCCTGGAAGAGAGGGTGCATTGTGAGGCAAGTCC  
CAAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTCTTTGTTCCCATTTATCCAAATAACTTGGACAGAGCA  
GCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCCAACCTGGGAATCAGAGAGAGAAGGAGAAGGAGGG  
GAGCCTGTCCGTTTCAGAGCCTCTGGCTGCATAGAAAAGGATTCTGGTGCTTCCCTGTTTGGCTGGCAGCAAGG  
GTTCCACGTGCATTTGCAATTTGCACAGCTAAATTTGCAGCATTTCCTCCAGCTGGGCTGTCCCAATGTTACCA  
TTTGAGATGCTCCAGGCTCCTAAGAGAATCCACCTCTCTGGCCCTGGGACATTGCAAGCTGCTACAAATAA  
ATTCTGTGTTCTTTTGACATAGCGTCATTGCCAAGTGACATCAGTGAGCCTCTTGAATCTGTTAGTCTCCT  
TTTTCAACAAAGGAGTGTGTTGAGAAAAGGAGAGAGGCTGAGATCATTAGGAGTTTGTGGGCGAGCAAGCA  
TGGAGCTTCTTGACAAATTTCTGGGTCCATAAACAAACCCCAAGTCCCTGCTGATCCAGTAGCCCTGGAGGTT  
CCCCAGGTAGGGAGAGCCAGAGGTGCCAGCCTTCTGAAGGGCCAGAAAATTTAGCCTGGATCTCCTCTTTTAC  
CTGCTAGGACTGGAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTCTCTGCTTGAGGTATTGCCCTGTGTG  
GAATTGAGTGCTCATGGGTGGCCTCATATCAGCCTGGGAGTTATTTTGATATGTAGAATGCCAGATCTTCCA  
GATTAGGCTAAATGTAATGAAAACCTCTTAGGATTATCTGTGGAGCATCAGTTTGGGAAGAATTATTGAATTAT  
CTTGCAAGAAAAAGTATGTCTCACTTTTGTAAATGTTGCTGCCTCATTGACCTGGGAAAAATGAAAAAAA  
AATAAAGCAATGGTAAGACCTTAAAAAAAAGAAAAAAAAGAAAAAAAAGAAAAAAAAGAAAAAAAAGAAAA

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**FIGURE 36**

MSRPGTATPALALVLLAVTLAGVGAQGALEDPDYYGQEIWSREPYARPEPELETFSPLP  
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDHS  
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA  
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHTWVTVKNGSGDMIF  
EGNSEKEIPVLNELPVPMPVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT  
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF  
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNDGYEKAYEGG  
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA  
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSAST  
HRLMTDARRRVCHTEDEFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES  
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKIPNAIISVEGINHDIRTANDGDYWRLL  
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTLSTNMARIREIMEKFGKQPVSLPARR  
LKLGRGRRRQRG

**FIGURE 37**

CTAAGAGGACAAGATGAGGCCCGGCTCTCATTTCTCCTAGCCCTTCTGTTCTTCCCTTGGCCAAGCTGCAGGGG  
ATTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTCCCAGGTGTTGACTCCAGCTCCAGC  
TTCAGCTCCAGCTCAGGTCGGGCTCCAGCTCCAGCCGACGCTTAGGCAGCGGAGGTTCTGTGTCCCAGTTGTT  
TTCCAATTTACCGGCTCCGTGGATGACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTT  
CCGTGGACAGATGGAAACGCTTGAATTCACAGCTCATGTCTTTCTCAGAAGTTTGAGAAAAGAACTTTCTAAA  
GTGAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAAACTGTTAAACCTAACTGTCCGAATTGACATCAT  
GGAGAAGGATACCATTTCTTACACTGAACCTGGACTTCGAGCTGATCAAGGTAGAAGTGAAGGAGATGGAAAAAC  
TGGTCATACAGCTGAAGGAGAGTTTTTGGTGAAGCTCAGAAAATTGTTGACCAGCTGGAGGTGGAGATAAGAAAT  
ATGACTCTCTTGGTAGAGAAGCTTGGACACTAGACAAAAACAATGTCTTGGCATTGCGCCGAGAAATCGTGGC  
TCTGAAGACCAAGCTGAAAGAGTGTGAGGCCCTTAAAGACTCAAAACACCCCTGTGCTCCACCCCTCTCCCACT  
CAGGGAGCTGTGGTCACTGGTGGTGTGGTGAACATCAGCAAAACGCTCTGTGGTTGAGCTCAAGTGGAGAGGGTTT  
TCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTCCCCAGCATCCAAACAAAGGACTGTATTGGGTGGCGCC  
ATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTACAACACACTGGATGATTGCTATTGTATATAA  
ATGCTCGAGAGTTGCCGATACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAAC  
ATGTACAACACCGGGAATATTGCCAGAGTTAACTTGACCACCAACACGATTGCTGTGACTCAAACCTCTCCCTAA  
TGCTGCCATAAATACCGCTTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGGATGAGAATG  
GATTGTGGGTTATTTATTCAACTGAAGCCAGCAGCTGGTAACATGGTGATTAGTAACTCAATGACACCACACTT  
CAGGTGCTAAACACTTTGGTATACCAAGCAGTATAAACCATCTGCTTCTAACGCCTTTCATGGTATGTGGGGTTCT  
GTATGCCACCCGTACTATGAACACCAGAAACAGAAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGG  
GCAAACTAGACATTGTAATGCATAAGATGCAGGAAAAAGTGCAGAGCATTAACATAACCCTTTTTGACCAGAAA  
CTTTATGTCTATAACGATGGTTACCTTCTGAATATGATCTTCTGTCTTGCAGAAGCCCCAGTAAAGCTGTTTA  
GGAGTTAGGTTGAAGAGAAAAATGTTTGTGAAAAAATAGTCTTCTCCACTACTTAGATATCTAGCGGGGTGT  
CTAAAAGTGTGTTTCATTTTGCAGCAATGTTTAGGTGCATAGTTCTACCACACTAGAGATCTAGGACATTTGTCT  
TGATTTGGTGAGTTCTCTTGGGAATCATCTGCCTCTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGA  
TTGTGAGAGTCTAGGGGCACTGTGGGCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTA  
GGAATTAAGGAATCTAAAACCTCAGTATGGCGCTAGGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAGTC  
CTCATCCATGTAGCACCCTAATTTCTCCATGCCTGGAAGAAACCTGGGCACTTAGTTAGGTAGATTAATATCT  
GGAGCTCCTCGAGGGACCAAACTCTCCAACTTTTTTTTCCCTCACTAGCACCTGGAAATGATGCTTTGTATGTGG  
CAGATAAGTAAATTTGGCATGCTTATATATTCTACATCTGTAAAGTGCTGAGTTTTATGGAGAGAGGCCTTTTT  
ATGCATTAATTTGTACATGGCAAATAAATCCCAGAAGGATCTGATAGTAGGCACCTGCTTTTTCTTTTCTCTC  
ATTGTCCACCTTACTAAAAGTCAGTAGAATCTTCTACCTCATAAATCTCTTCCAAAGGCAGCTCAGAAGATTAG  
AACAGACTTACTAACCAATTCACCCCCCAACACCCCTTCTACTGCCTACTTTAAAAAATTAATAGTTTTT  
CTATGGAAGTGTCTAAGATTAGAAAAATAATTTTCTTAATTTTCAATTAGGACTTTTATTACATGACTCTA  
AGACTATAAGAAAAATCTGATGGCAGTGACAAAGTGCTAGCATTTATTGTTATCTAATAAAGACCTTGGAGCATA  
TGTGCAACTTATGAGTGTATCAGTTGTTGCATGTAATTTTTGCCTTTGTTTAAAGCCTGGAACCTGTAAGAAAAAT  
GAAAATTTAATTTTTTTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGT  
TGGAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTTTGTCTATTTT  
TCCTTTGATGTTCAAGTCTAGTCTATGAGATTGGCAGTTTAAATGCTTTACTCCCCCTTTTAAATAAATGAT  
TAAATGTGCTTTGAAAAAATAAAAAAAAAAAAAAAAAA

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**FIGURE 38**

MRPGLSFL LALLFFLGQAAGDLGDVGPPIPSPGFS SFPGVDSSSSFSSSSRSGSSSSRSLGS  
GGSVSQLFSNFTGSVDDRGTCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV  
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ  
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH  
GGVVNISKPSVVQLNWRGFSYLYGAWGRDYSPQHHPNKGLYWVAPLNTDGRLL EYYRLYNTLD  
DLLLYINARELRITYGQGSGTAVYNNNMYVNM YNTGNIARVNLTNTIAVTQTL PNAAYNNR  
FSYANVAWQDIDFAVDENGLWVIYSTEASTG NMVISKLNDTTLQVLNTWYTKQYKPSASNAF  
MVCGLYATRMTMNRTEEIFYYYDTNTGKEGKL DIVMHKMQEKVQSINYNPFDQKLYVYNDG  
YLLNYDLSVLQKPQ

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**FIGURE 39**

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTCGTCCAC  
CCTCCTCCCCTCCAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT  
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC  
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG  
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT  
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACA  
TGTACAACACCGGGNATATTGCCAGAGTTAACCTGACC

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**FIGURE 40**

TCTCGCAGATAGTAAATAATCTCGGAAAGGCGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT  
CCGCTGCTCTTGTGACGTTGTGGAGATGGGGAGCGTCTGGGGCTGTGCTCCATGGCGAGCT  
GGATACCATGTTTGTGTGGAAGTGCCCCGTGTTTGCTATGCCGATGCTGTCTAGTGGAAC  
AACTCCACTGTAAC TAGATTGATCTATGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTG  
TGTAATGTTGATACCAGGAATGGAAGAACAACGAATAAGATTCCTGGATTTTGTGAGAATG  
AGAAAGGTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT  
GGTTTGGCTATGTTCTATCTTCTTCTCTTACTAATGATCAAAGTGAAGAGTAGCAGTGA  
TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA  
TTATTGGGGCATTCTTCATTCCAGAAGGAACTTTACAACGTGTGTGGTTTTATGTAGGCATG  
GCAGGTGCCTTTTGTTCATCCTCATACAACAGTCTTACTTATTGATTTTGCACATTCATG  
GAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGAACCTCGAGATGTTGGTATGCAGCCTTGT  
TATCAGCTACAGCTCTGAATTATCTGCTGTCTTATGTTGCTATCGTCTGTTCTTTGTCTAC  
TACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGCGTTTCATCAGTGTCAACATGCTCCTCG  
CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT  
TGTTACAGTCTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT  
GAACCAGAAACAAATTGCAACCCAAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC  
TGTCCCAAAGGAAGGGCAGTCAAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC  
TCTTTTGTGTGTGTATTTTATTCCAGCATCCGTACTTCAAACAATAGTCAGGTTAATAAA  
CTGACTCTAACAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC  
ACTGGAGGATGGGGACGATGTTCCCGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA  
GTTATTCCTTCTTCACTTCATGCTTTTCTGGCTTCACTTTATATCATGATGACCCCTTACC  
AACTGGTCCAGGTATGAACCCCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA  
AATCTCTTCCAGTTGGATTGGCATCGTGTGTATGTTTGGACACTCGTGGCACCCTTGTTC  
TTACAAATCGTGATTTTGAAGTGAAGTGAAGTCTAGCATGAAAGTCCCACTTTGATTATTGC  
TTATTTGAAAACAGTATTCCCACTTTTGTAAAGTTGTGTATGTTTTTGGCTTCCCATGTAAC  
TTCTCCAGTGTCTGGCATGAATTAGATTTTACTGCTTGTCAATTTTGTATTTTCTTACCAA  
GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT  
TAGTAAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAATGAAGAGTAAAA  
ACAAATTTGTTTGACTATTTTAAAATTATATTAGACCTTAAGCTGTTTTAGCAAGCATTA  
GCAAATGTATGGCTGCCTTTTGAATATTTGATGTGTTGCCTGGCAGGATACTGCAAGAAC  
ATGGTTTATTTTAAAATTTATAAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA  
AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTTTAGTGGACAATAGTGTAGG  
TTATGGATGGAGGTGTCGGTACTAAATTGAATAACGAGTAAATAATCTTACTTGGGTAGAGA  
TGGCCTTTGCCAACAAAGTGAAGTGTTTTGGTTGTTTTAACTCATGAAGTATGGGTTCACT  
GGAAATGTTTGGAACTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGA  
AGGAAGTGTTTGAAAGTCACTTTGAAAGTTAGTTTTGGGCCAGCACGGTAGCTCACCCTT  
GGTAATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCCAGGAATTCAGACCA  
GCTTGGCACATGGTGAACCTGTTCTATAAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTC  
CAGCACTGAGAGGCTAGTGAAGATTGCTGAGCCAGAGCCAAAGGTTGCAGTGAGCAAGTCA  
CGTCACTGCACTCTAGCTGGCACAGAGTAAGCCAAAAAATATATATATATTGAAATCAAGG  
AGGCAAAATTTTGACAGGGAAGGAAGTAAGTGAACCAACTAGGCTTTAGTAGGTACTTAT  
ATAAAATCTAGTCCAGTTCTCTCATTTTAAAAAATGAAGACACTGAAATACAGACTTAAATA  
GCTCAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTGACATTTAA  
AAATAATTTCTATTCAAATACATGCATATTGATTTACACCTCATACTGTGATAATTAATGT  
GATGTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTCAGAAGAATGATGGAATGTTTT  
AGAATAAACTCCTGCTTATAGTATACTACACAGTTCAAAAGATGTTTAAATGCTTTTGTAT  
TTACTGCCATGTAATTGAAATATATAGATTATTGTAACCTTCAACCTGAAAATCAAGCAGT  
ATGAGAGTTTATGTTATTTGTATGTGTCTAGTAGTCTAATGAAGCTTTTAAATCTACAATT  
TCTTCTTTAAAAATTTTATTAATGTGAATGGAATATAACAATTCAGCTTAATTTCCCAACC  
TTATTCTGTGTGTAGACATTGTATTCCACAATTTTGAATGGCTGTGTTTTACCTCTAAATAA  
ATGAATTCAGAGAAAAA

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**FIGURE 41**

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME  
EQLNKIPGFCENEKGVVPCNILVGKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG  
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQLVLLIDFAHSWNESWVEKM  
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI  
LPKIQESQPRSGLLQSSVITVYTMYLTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV  
QWWHAQGIIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH  
RAVDNERDGVTSYSFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVVWKISSSWIGI  
VLYVWTLVAPLVLTNRDFD



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**FIGURE 42**

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT  
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCC  
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAAACAANTCCACTGTAAGTAGATTGATCTA  
TGCACTTTTCTTGCTTGTTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG  
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT  
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCT  
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT  
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

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**FIGURE 43**

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC  
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNTATGCCGATGCTGTCCTAGTGGAAACAANTCC  
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT  
GTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG  
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG  
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG  
AGCTGCAGTGCACAATGGATTTTGGTTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG  
GGGC

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**FIGURE 44**

AAGAAGCTGTCTCCATCTTGTCTGTATCCGCTGCTCTTGTGAACGTTNTGGAGATGGGGAGC  
GTCCTTGGGGTTGTGCTCCATGGCGAGCTGGATACCATGTTTGTGTGGAAGTGCCCCGTGTT  
TGCTATGCCGATGCTGTCCTAGTGGAAACAACCTCCACTGTAAGTAGATTGATCTATGCACTT  
TTCTTGCTTGTGGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAAC  
GAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATTTTGGTTG  
GCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTTTA  
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTT  
CTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

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**FIGURE 45**

GCTGTCCTTAGTGGAAACAANTCCAACCTTGTAACCTGGATTGATCTATGCACTTTTTTCCTTG  
CTTGTTGGAGTATGTGTAGCTTTGTGTAATGTTGTTCCCAGGATTGGANGAACAACTGAATA  
AGATTCCTGGATTTTTGTGAGAATGAGAAAGGTGTTGTCCCCTTGTAACATTTTTGGTTGGC  
TATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTCTCTTTACT  
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCT  
TTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTTCATTCCAGAAGGAACCTTT  
ACAACTGTGTGGTTTTATGTAGGCATGGCAGGTGCCTTTTGTTTCATCCTCATACTAGT  
CTTACTTATTGATTTTGCACATTCATGGAATGAATCGTGGGTTGAAAAATGGAAGAAGGGA  
ACTCGAGATGTTGGTATGCAGCCTTGTTATCAGCTACAGCTCTGAATTATCTGCTGTCTTTA  
GTTGCTATCGTCCTGTTCTTTGTCTACTACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGC  
GTTTCATCAGTGTCAACATGCTCCTCTGCGTTGGTGCTTCTGTAATG

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**FIGURE 46**

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCCTGCGATTGAGCTGCGGGTCGCGGGCGGGCGCCGGCCTCTCCAAT  
GGCAAATGTGTGTGGCTGGAGGCGAGCGGAGGCTTTCGGCAAAGGCAGTCGAGTGTGTCAGACCGGGGCGAG  
TCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGTGTCTATTACGAGGGGAGCGCCGGCGGGGCTGTGCG  
ACTCCCCGCGGAACATTTTGCTCCCTCCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAGAGGCAGATTAC  
GTCGTTTCCAGCCAAGTGGACCTGATCGATGGCCCTCCTGAATTTATCAGCATATTTGATTTATTAGCGATGCC  
CCCTGGTTTGTGTGTTACGCACACACACGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGTTTCCAGCTCC  
TGGGCGAATCCACATCTGTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGAGAGTGTGTCGAATCTGCGAGTG  
AAGAGGGACGAGGGAAAAGAAACAAAGCCACAGACGCAACTTGAGACTCCCGCATCCCAAAAGAGCACCAGAT  
CAGCAAAAAAAGAAGATGGGCCCCCGAGCCTCGTGCTGTGCTTGTGCTCCGCAACTGTGTTCTCCCTGCTGGG  
TGGAAGCTCGGCCTTCCCTGTCGCACCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCA  
ACATCATCTGCTGCTGACGGACGACCAGGATGTGGAGCTGGGTTCATGCAGGTGATGAACAAGACCCGGCGC  
ATCATGGAGCAGGGCGGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATGTGCTGCCCTCAGCTCCTC  
CATCTCACTGGCAAGTACGTCCACAACCACAACCTACACCAACAATGAGAACTGCTCCTCGCCCTCCTGGC  
AGGCACAGCAGAGAGCCGACCTTTGCCGTGTACCTCAATAGCACTGGCTACCGGACAGCTTTCTTCGGGAAG  
TATCTTAATGAATACAACGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTGCGACTCCTTAAAAAATCCCG  
CTTTTATAACTACAGCTGTGTGGAACGGGGTGAAGAGAAGCAGGCTCCGACTACTCCAAGGATTACCTCA  
CAGACCTCATACCAATGACAGCGTGAGCTTCTTCGCACGTCCAAGAAGATGTACCCGCACAGGCCAGTCTCT  
ATGGTCATCAGCCATGCAGCCCCCAGGCCCTGAGGATTACGCCCCACAATATTACGCCTCTTCCCAAACGC  
ATCTCAGCACATCAGCCGAGCTACAACCTACGCGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGG  
CCATGAAGCCCCATCCACATGGAATTCACCAACATGCTCCAGCGGAAGCGCTTGCAGACCCCTCATGTGCGTGGAC  
GACTCCATGGAGACGATTTACAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACACCGC  
CGACCACGGTTACCACATCGGCCAGTTTGGCCTGGTGAAAGGGAAATCCATGCCATATGAGTTTGACATCAGGG  
TCCCGTTCTACGTGAGGGGCCCCAACGTGGAAGCCGGCTGTCTGAATCCCCACATCGTCTCAACATTGACCTG  
GCCCCACCATCCTGGACATTGCAGGCCTGGACATACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGT  
GGACACGGAGCGGCCGCTGAATCGGTTTCACTTGAAAAGAAAGATGAGGGTCTGGCGGACTCCTTCTTGGTGG  
AGAGAGGCAAGCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCCAGGAGGAGAACTTTCTGCCAAGTAC  
CAGCGTGTGAAGGACCTGTGTACGCTGTGAGTACCAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTG  
TGTGGAGGACGCCACGGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCCCATGCGGTGGGCGGCAGCAGAGCCC  
TCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCAGCGAGGCTGCACCTGTGACAGCGGGGACTACAAGCTC  
AGCCTGGCCGGACGCGGAAAAAATCTTCAAGAAAGAAAGTACAAGGCCAGCTATGTCCGCACTCGCTCCATCCG  
CTCAGTGGCCATCGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGGTGATGCCGCCAGCCCCGAAACCTCA  
CCAAGCGGCACTGGCCAGGGGCCCCCTGAGGACCAAGATGACAAGGATGGTGGGACTTCAGTGGCACTGGAGGC  
CTTCCCGACTACTCAGCCGCCAACCCCATTAAGTGACACATCGGTGCTACATCCTAGAGAACGACACAGTCCA  
GTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGAAGACCACAAGCTGCACATCGACCACGAGATTGAAA  
CCCTGCAGAACAAAATTAAGAACCTGAGGGAAGTCCGAGGTACCTGAAGAAAAGCGGCCAGAAGAATGTGAC  
TGTCACAAAATCAGTACCACACCCAGCACAAAGGCCGCCCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTCAG  
GAAGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAACTCCGCAAGCTGC  
TCAAGCGCCTGCAGAACAACGACACGTGCAGCATGCCAGGCCTCACGTGCTTACCCACGACAACCAGCACTGG  
CAGACGGCGCCTTCTGGACACTGGGGCCTTCTGTGCTGCACCAGCGCCAACAATAACACGTACTGGTGCAT  
GAGGACCATCAATGAGACTCACAATTTCTTCTGTGAATTTGCAACTGGCTTCTAGAGTACTTTGATCTCA  
ACACAGACCCCTACCAGCTGATGAATGCAGTGAACACACTGGACAGGGATGTCTCAACCAGCTACACGTACAG  
CTCATGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAAACCCCGGACTCGAAACATGGACCTGGATGGAGG  
AAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAGACCTTCTTCCAAATCACTGG  
GACAACCTGTGGGAAGGCTGGGAAGGTTAAAGAAACAACAGAGGTGGACCTCCAAAAACATAGAGGCATCACCTGA  
CTGCACAGGCAATGAAAAACCATGTGGGTGATTTCCAGCAGACCTGTGCTATTGGCCAGGAGGCCTGAGAAAGC  
AAGCACGCACTCTCAGTCAACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCC  
ATTTTTGCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAAAAAGTC  
ACCACTAACCTCCCCAGAAGCTCACAAGGAAAACGGAGAGAGCGAGAGAGATTTCCTTGGAATTTTC  
TCCCAAGGGCGAAAGTCATTGGAATTTTAAATCATAGGGGAAAAGCAGTCTGTCTAAATCCTCTTATCTT  
TTGGTTTGTACAAAAGAAGGAACATAAGAAGCAGGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACG  
TTTGACAATGAGTCAGTAGCACAAAAGAGATGACATTTACCTAGCACTATAAACCTGGTTGCCTCTGAAGAAA  
CTGCCTTCATGTATATATGTGACTATTTACATGTAATCAACATGGGAACCTTTAGGGGAACCTAATAAGAAAT  
CCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAAGAAAA

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**FIGURE 47**

MGPPSLVLCLLSATVFSLLGGSSAFLSHRLKGRFQRRRNIRPNIIILVLTDDQDVELGSMQ  
VMNKTRRIMEQGGAHFINAFVTTMCCPSRSSILTGKYVHNHNTYTNNENCSSPSWQAQHE  
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD  
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP  
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT  
YIVYTADHGYHIGQFGLVKGKSMPEYFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI  
AGLDIPADMDGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVD AQEEN  
FLPKYQRVKDLQRAEYQTACEQLGQKWQCVEDATGKLKLHKCKGPMRLGGSRALSNLVPKY  
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSV AIEVDGRVYHVGLGDAAQ  
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQC DL DLYKS  
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGR LKH RGSSL  
HPFRKGLQEKDKVWLLREQRKKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG  
PFCACTSANNNTYWCMRTINETHNFLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL  
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

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**FIGURE 48**

AACAAAGTTCAGTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA  
GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAGATGCTGGGCCTCCTGGGGAGCACAGCCC  
TCGTGGGATGGATCACAGGTGCTGCTGTGGCGGTCTGCTGCTGCTGCTGCTGCTGGCCACC  
TGCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGGAAA  
CCGAGTCCGCCGGGGCCAGCCTTGGCCCTTCCGGCGGGGGGCCACCTGGGAATCTTTCACC  
ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC  
CCCCGCCACACCCCTCACCACCTCCACCACCACCACCACCCCCACCGCCACCATCCCCGCCA  
CGCTCGCTTGAAGGCTGCTGTGCGCCGGTGCCTGTGGACAGCAGCTGCCCCTGCCCTCCCATCTG  
TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG  
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTA CTATGGC  
AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG  
GTGCTCTTTCCGGGGCTGGACAGCCCGTCTTGTGACAGTGACTCCCAGTGAGCCCCAGAAATG  
ACAAGCGTGTCTTGGCAGAGCCAGCACACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC  
ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT  
GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTCATCGGTGCCTTAGTCCAAGAAAAT  
AAAAACCACTAAGAAGCTTTAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 49**

MLGLLGSTALVGWITGA AVAVLLLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAPWPFR  
RRGHLGIFHHHRHPGHVSHVPNVGLHHHHHPRHTPHHLHHHHHPRHHPRHAR



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**FIGURE 50**

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCC**ATG**TCGGACCTGCTA  
CTACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTGCCGG  
GTACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTCACCCCCCATCCGCAACGTCA  
CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC  
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC  
CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC  
CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC  
CATGTGGTGACAGCCACCTTCCCCTACACCACCATTCTGTCCATCTGGCTGGCTACCCGCCG  
TGTCCATCCTGCCTTGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG  
AGATCTACCAGGAAGACCAGATCCATTTTCATGTGCCCACTGGCACGGCAGGGAGACTTCTAT  
GTGCCTGAGATGAAGGAGACAGAGTGGAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA  
GGTGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAGTGAGCC  
CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTCACCTGGGGCGAGCAGCCGTGGCTGGGAT  
GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA  
GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCCTGGGACTGAGC  
CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCTGAGAAGGGCAAGGAG**TAA**CCC  
ATGGCCTGCACCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT  
CCAGCCCTCTCCTCCTCCTCTGGGGGAGGAGGGGTTCTTGAGGGACCTGACTTCCCCTGC  
TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA  
GGGACTATTTTCTGCACCAGCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTCAGACTC  
ACAGTGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTACCTGGAAAAAA  
AAAAA

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**FIGURE 51**

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGlyGETGR  
LFTESCSISPKLRSIAVYYDNPHMVPPDKCRAVGSILSEGEESPSPELIDLYQKFGFKVFS  
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPAR  
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAA TLSPGAS  
SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGLGESRLDPGTEPLGTTKWLWEPTAPEK  
GKE

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**FIGURE 52**

CCGCGGGAACGCTGTCCTGGCTGCCGCCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCT  
GCCCCGCGCCCAAGTC**ATG**ACCCTGCGCCCCCTACTCCTCCCGCTCCATCTGCTGCTGCTGCT  
GCTGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGA  
CCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGA  
GACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCT  
GACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGA  
GTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTAT  
GGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCT  
GATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTGCTGCTCTGGTAG  
GGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAAT  
AGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAA**TA**  
**A**TAAATAATAAATTTTAAAAAACTTAAAAAAAAAAAAAAAAAAAA

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**FIGURE 53**

MTLRPSLLPLHLLLLLLLLLSAAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGDTLHI  
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF  
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS  
KKKLKEEKRNKS KKK

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**FIGURE 54**

CCCGGGAACGTGTTCTGGCTGCCGCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCTGC  
CCCGCGCCCAGTCATGACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCTGC  
TGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGACC  
CTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGAGA  
CACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCTGA  
CCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT  
CTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCTTCTCACTTGGCCTATGG  
AAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCTGA  
TTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTCTTGCCTCTGGTAGGG  
ATGGCCATGGTGCCACCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAATAGA  
CCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAAATAATA  
AATAATAAATTTTAAAAAACTTA

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**FIGURE 55**

CCGAAAGTCCCGTCCGGACCCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC  
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG  
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA  
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT  
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT  
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGG  
GCATTTTGCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC  
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAA  
CAAGAGCAAAAAGAAATAATAAATAATAAATTTTAAAAAACTTAAAA

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**FIGURE 56**

CTGCTGCATCCGGGTGTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAATCGGGGGAG  
TGAGGCGGGCCGGCGCGGCGGACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG  
ACCTGAAAAAAATGCTCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG  
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT  
TATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCT  
GTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA  
GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG  
TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG  
CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT  
TTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGACTTATGGCAGTGAACACATCTGAT  
TTCCACAGCACAACAGCCCTGCATGGGTTTGTGTTTTTTTACTGCTCACTCCCAACCTT  
TTGTAATGCCATTTTCTAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT  
AAAATCACGAGAACACCTAAACAACAACCAAAAATCTATTGTGGTATGCACCTTGATTAACCT  
ATAAAATGTTAGAGGAACTTTCACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT  
TGTAATAATAAAAAGAAATTACAAAAGAAATTATGGATTTGTCAATGTAAGTATTTGTCATA  
TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT  
CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAATATTCCGTGG  
TCAAATTTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT  
GTAAGTGGCTTTTGAGGGTCTCCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT  
GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT  
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTTCTGGTGGGATGCACAGTCACTC  
CACATCCACCACTG

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**FIGURE 57**

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWIIIDA AVIYPTMKDFNHSYHACGVI  
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK  
DIVYPGIAVFFQNAFIFFGGLVFKFGRTE DLWQ



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**FIGURE 58**

TTCTTGGCTAAAATCGGGGGAGTGAGGCGGGCCGGCGCGGCGACACCGGGCTCCGGAACC  
ACTGCACGACGGGGGCTGGACTGACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATG  
CTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC  
TATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGAT  
TTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGC  
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTG  
CTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGG  
ATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATT  
TTCCAGAATGCCTTCATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGC

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**FIGURE 59**

TGGACGGACCTGAAAAAATGTTTGGATTTNTAGAGGGNTTGAGATGTTTCAGAATGCATGAC  
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG  
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC  
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA  
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTGTTGGCTTTT  
CGTTGGTTTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTTGGAGGTT  
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC  
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

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**FIGURE 60**

GGACACCGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAATGTTTGGATT  
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT  
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT  
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGC  
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT  
GTTTGGGTCAAACAGGTGNTCGCATTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT  
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT  
ACCCTGGAATTNCTNTATTTTTCCAGAATGCC

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**FIGURE 61**

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC  
ATTGNTGNTGGTGTANTATTTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT  
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC  
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG  
TTTGGGTCAAACAGGTGNTNGCATTTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN  
TGATTGCATTTATGTGGATTNTTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC  
CCTGT

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**FIGURE 62**

GGGAGGCTGTGNCCGTTTTGTTTTNTTGGCTAAAATCGGGGGAGTGAGGCGGCCCGGCGCGG  
CGNGACACCGGGTTCCGGGAACCATTGCACGACGGGGTGGACTGACCTGAAAAAAATGTTTG  
GATTTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATT  
GCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT  
TATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCA  
TAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA  
GGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGG  
ATNTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAG  
TATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATNTTTTTTGGAGGGCTG

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**FIGURE 63**

CGACGCCGGCGTG**ATG**TGGCTTCCGCTGGTGCTCCTGGCTGTGCTGCTGCTGCTGGCCGTCC  
TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC  
AAACGGCCCCCAGCGCCCCCTGGTAACTGACAAGGAGGCCAGGAAGAAGGTTCTCAAACAAGC  
TTTTTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG  
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCCTGGTGCTGGAACAACAT  
ACCAAGGCAGGGGGCTGCTGTCATACCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT  
CCATTACATTGGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG  
AAGGGCAGCTGGACTGGGCTCCCCTGTCTCTCTCTCTTTGACATCATGGTACTGGAAGGGCCC  
AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTCAGGGCCTCAAGGA  
GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA  
GTGGAGCCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCGTGGTTTCAGCTCCTCGAC  
AGGTGTGGGCTGCTGACTCGTTTCTCTCCATTCTCTCAAGCATCCACCCAGAGCCTGGCTGA  
GGTCTGCAGCAGCTGGGGGCCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA  
CTTACGGTGTCACCCCCAACCACAGTGCCTTTTCCATGCACGCCCTGCTGGTCAACCACTAC  
ATGAAAGGAGGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT  
GATTACAGCGGGCTGGGGGCGCTGTCTCACAAGGCCACTGTGCAGAGTGTGTTGCTGGACT  
CAGCTGGGAAAGCCTGTGGTGTGCTAGTGTGAAGAAGGGGCATGAGCTGGTGAACATCTATTGC  
CCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCGGGGGAACGC  
CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCGGCCCGGCTTAGGCATGACCT  
CTGTTTTTCATCTGCCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT  
GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCCAGGGAAGA  
GGCTGCGGAACACATCCCTCTTCTCTTCTTCTCGCTTTCCCATCAGCCAAAGATCCGAGCTGGG  
AGGACCGATTCCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT  
GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGGCAGTGAATGAGACCTTCAAAAACCTC  
CTTTGTGGAAGCCTCTATGTGCTAGTGGTCTTGAAGTGTTCACACAGCTGGAGGGGAAGGTGG  
AGAGTGTGACTGCAGGATCCCACTCACCACAGTCTATCTGGCTGCTCCCCGAGGTGCC  
TGCTACGGGGCTGACCATGACCTGGGCGCCTGCACCCCTGTGTGATGGCCTCCTTGAGGGC  
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTACCTGTGGACTGGTGC  
GGGCCCTGCAAGGTGCCCTGCTGTGACAGCAGCGCCATCCTGAAGCGGAACCTGTACTCAGAC  
CTTAAGAATCTTGATTCTAGGATCCGGGCACAGAAGAAAAAGAAT**TAG**TTCCATCAGGGAGG  
AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG  
CATTAGTTCTTGCACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCTAG  
TTTAAATCACAATTCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA  
TCTTTACGCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG  
TCTCATGACGAGCGGGCCTCTGCATCCCTCACCCTGCTTCACTCAGTGATCAAAGCGA  
ATATTCCATCTGTGGATAGAACCCCTGGCAGTGTTGTGCTCAGCTCAACCTGGTGGGTTCAAGT  
TGCTCTGAGGCTTCTGCTCTCATTCTTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG  
GAAAAGGGAGACTAATGAGGCTTAACCTCAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA  
GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTCACTGGCTCTTCAGGGGACAGGAAT  
GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA  
GGGTGCATGTGAGATGATCATATCCAATTCATATGGAAGTCCCGGGTCTGTCTTCTTATCA  
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGGACTCAGTACCTGAGCCTCAATCAAGC  
CTTATCCACCAATAACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA  
TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG  
CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAGGGGAAGTCACATCAGAAAAGGGA  
AAGCCACGGAATGTGTGTGAAGCCCAGAAATGGCATTTCAGTTAATTAGCACATGTGAGGG  
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTCAGTTATGTCTTTG  
GTATCAGACATACGAAAGGTCTCTTTGTAGTTTCGTGTTAATGTAACATTAATAAATTTATTG  
ATTCCATTGCTTTAAAAA

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**FIGURE 64**

MWLPLVLLLAVLLLAVLCKVYLG LFSGSSPNPFSEDVKRPPAPLVTDKEARKKVLKQAFSAN  
QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG  
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ  
EEAIIDKYIKLVKVVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ  
LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA  
GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPIVVSNAGLFNTYEHLLPGNARCLP  
GVKQQLGTVRPGLGMTSVFICLRGTKEDLHLPSTNYYVYYDTMDQAMERYVSMPREEAAEH  
IPLLEFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAEKKGKRGSDYETFKNSFVEA  
SMSVVLKLFPPQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI  
PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

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FIGURE 65

GCAGCGGCGAGGCGGCGGTGGTGGCTGAGTCCGTGGTGGCAGAGGCCAAGGCCGACAGCTCTA  
GGGGTTGGCACCGGCCCGAGAGGAGGATGCGGGTCCGGATAGGGCTGACGCTGCTGCTGTG  
TGCGGTGCTGCTGAGCTTGGCCTCGGCGTCTCGGATGAAGAAGGCAGCCAGGATGAATCCT  
TAGATTCCAAGACTACTTTGACATCAGATGAGTCAGTAAAGGACCATACTACTGCAGGCAGA  
GTAGTTGCTGGTCAAATATTTCTTGATTGAGAAGAATCTGAATTAGAATCCTCTATTCAAGA  
AGAGGAAGACAGCCTCAAGAGCCAAGAGGGGGAAAGTGTACAGAAGATATCAGCTTTCTAG  
AGTCTCCAAATCCAGAAAACAAGGACTATGAAGAGCCAAAGAAAGTACGGAAACCAGCTTTG  
ACCGCCATTGAAGGCACAGCACATGGGGAGCCCTGCCACTTCCCTTTTCTTTTCTTAGATAA  
GGAGTATGATGAATGTACATCAGATGGGAGGGAAGATGGCAGACTGTGGTGTGCTACAACCT  
ATGACTACAAAGCAGATGAAAAGTGGGGCTTTTGTGAACTGAAGAAGAGGCTGCTAAGAGA  
CGGCAGATGCAGGAAGCAGAAATGATGTATCAAATGGAATGAAAATCCTTAATGGAAGCAA  
TAAGAAAAGCCAAAAAAGAGAAGCATATCGGTATCTCCAAAAGGCAGCAAGCATGAACCATA  
CCAAAGCCCTGGAGAGAGTGTATATGCTCTTTTATTTGGTGATTACTTGCCACAGAATATC  
CAGGCAGCGAGAGAGATGTTTGAGAAGCTGACTGAGGAAGGCTCTCCCAAGGGACAGACTGC  
TCTTGGCTTTCTGTATGCCTCTGGACTTGGTGTTAATTCAAGTCAGGCAAAGGCTCTTGTAT  
ATTATACATTTGGAGCTCTTGGGGGCAATCTAATAGCCACATGGTTTTGGTAAGTAGACTT  
TAGTGGAAGGCTAATAATATTAACATCAGAAGAATTTGTGGTTTATAGCGGCCACAACTTTT  
TCAGCTTTCATGATCCAGATTTGCTTGATTAAGACCAAATATTCAGTTGAACTTCCTTCAA  
ATTCTTGTTAATGGATATAACACATGGAATCTACATGTAAATGAAAGTTGGTGGAGTCCACA  
ATTTTTCTTTAAATGATTAGTTTGGCTGATTGCCCCATAAAAGAGAGATCTGATAAATGGC  
TCTTTTTTAAATTTTCTCTGAGTTGGAATTGTCAGAATCATTTTTTTACATTAGATTATCATAA  
TTTTTAAAAATTTTTCTTTAGTTTTTCAAATTTTTGTAAATGGTGGCTATAGAAAAACAACAT  
GAAATATTATACAATATTTTGCAACAATGCCCTAAGAATTGTTAAATTCATGGAGTTATTT  
GTGCAGAATGACTCCAGAGAGCTCTACTTTCTGTTTTTTACTTTTCATGATTGGCTGTCTTC  
CCATTTATTCTGGTCATTTATTGCTAGTGACACTGTGCCTGCTTCCAGTAGTCTCATTTTTCC  
CTATTTTGCTAATTTGTTACTTTTTCTTTGCTAATTTGGAAGATTAACATTTTTTAATAAA  
ATTATGTCTAAGATTAAAAA  
AAAAA



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**FIGURE 66**

MRVRIGLTLLLCVLLSLASASSDEEGSQDES LDSKTTLTSDSVKDHTTAGRVVAGQIFLD  
SESELESSIQEEEDSLKSQEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG  
EPCHF PFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEAARRQMQAEMM  
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERSYALLFGDYLPQNIQAAREMF EK  
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLI AHMVLVSRL

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**FIGURE 67**

CTTCCCAGCCCTGTGCCCCAAAGCACCTGGAGCATATAGCCTTGCAGAACTTCTACTTGCCT  
GCCTCCCTGCCTCTGGCCATGGCCTGCCGGTGCCTCAGCTTCCTTCTGATGGGGACCTTCCT  
GTCAGTTTCCCAGACAGTCCTGGCCCAGCTGGATGCACTGCTGGTCTTCCCAGGCCAAGTGG  
CTCAACTCTCCTGCACGCTCAGCCCCCAGCACGTCACCATCAGGGACTACGGTGTGTCCTGG  
TACCAGCAGCGGGCAGGCAGTGCCCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA  
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCCACAATGCCT  
GTGTCCTCACCATTAGTCCCGTGCAGCCTGAAGACGACGCGGATTACTACTGCTCTGTTGGC  
TACGGCTTTAGTCCCTAGGGGTGGGGTGTGAGATGGGTGCCTCCCCCTCTGCCTCCCATTCT  
GCCCCTGACCTTGGGTCCCTTTTAAACTTTCTCTGAGCCTTGCTTCCCCTCTGTAAAATGGG  
TTAATAATATTCAACATGTCAACAAC

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**FIGURE 68**

MACRCLSFLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG  
SAPRYLLYYRSEEDHHRPADI PDRFSAKDEAHNACVLTISPVPEDDADYYCSVGYGFSF

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**FIGURE 69**

CCCGCCCCGCCCCGAGACCGGGCCCCGGGGGCGCGGGGCGGGGATGCGGGCGCCCGGGGGCGG  
CGATGACCGCGGAGCGCACGCCGCGGGCCCCGGCCCTGACCCCCGCGCCCGCCCGCTGAGCCC  
CCCCCGGAGGTCCGGACAGGCCGAG**ATG**ACGCCCGAGCCCCCTGTTGCTGCTCCTGCTGCCGC  
CGCTGCTGCTGGGGGCTTCCCACCGGCCCGCCGCCCGGAGGCCCCCAAAGATGGCGGAC  
AAGGTGGTCCCACGGCAGGTGGCCCCGGCTGGGCGCACTGTGCGGCTGCAGTGCCAGTGGA  
GGGGGACCCGCGCCGCTGACCATGTGGACCAAGGATGGCCGCACCATCCACAGCGGCTGGA  
GCCGCTTCCGCGTGCTGCCGCAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC  
GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCCTGAGCGTCAACTACACCCCTCGTCGT  
GCTGGATGACATTAGCCCAGGGAAGGAGAGCCTGGGGCCCGACAGCTCCTCTGGGGGTCAAG  
AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC  
CGGGTGATCGCACGGCCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGCCAGCGGGCACCC  
TCGGCCCCGACATCACGTGGATGAAGGACGACAGGCCCTTGACGCGCCAGAGGCGCTGAGC  
CCAGGAAGAAGAGTGGACACTGAGCCTGAAGAACCCTGCGGCCGGAGGACAGCGGCAAATAC  
ACCTGCCGCGTGTCGAACCGCGCGGGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA  
GCGGACCCGTTCCAAGCCCGTGCTCACAGGCACGCACCCCGTGAACACGACGGTGGACTTCG  
GGGGGACCACGTCCTTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG  
AAGCGCTGGAGTACGGCGCCGAGGGCCGCCACAACCTCACCATCGATGTGGGCGGCCAGAA  
GTTTGTTGGTGCTGCCACGGGTGACGTGTGGTTCGCGGCCCGACGGCTCCTACCTCAATAAGC  
TGCTCATCACCCGTGCCGCGCAGGACGATGCGGGCATGTACATCTGCCTTGGCGCCAACACC  
ATGGGCTACAGCTTCCGCGAGCGCCTTCCTCACCGTGCTGCCAGACCCAAAACCGCCAGGGCC  
ACCTGTGGCCCTCCTCGTCCTCGGCCACTAGCCTGCCGTGGCCCGTGGTTCATCGGCATCCAG  
CCGGCGCTGTCTTCATCCTGGGCACCCCTGCTCCTGTGGCTTTGCCAGGCCGAGAAGCCG  
TGCACCCCGCGCCTGCCCTCCCCTGCCCTGGGCACCGCCCGCCGGGGACGGCCCGCGACCG  
CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGTGTGGGGCTGT  
GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCCAGTTGCTGGC  
CCTAAGTTGTACCCCAAACCTACACAGACATCCACACACACACACACACACTCTCACAC  
ACACTCACACGTGGAGGGCAAGGTCCACCAGCACATCCACTATCAGTGCT**TAG**ACGGCACCGT  
ATCTGCAGTGGGCACGGGGGGGCGGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT  
GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCAGGCAGTCTGTGTG  
TGAGGCATAGCCCCCTGGACACACACACAGACACACACACTACCTGGATGCATGTATGCAC  
ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG  
CCGCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA  
TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGCTGCCTGGACA  
CACACACACACACGGATATGCTGTCTGGACGCACACACGTGCAGATATGGTATCCGGACACA  
CAGTGCACAGATATGCTGCCTGGACACACAGATAATGCTGCCTTGACACACACATGCACGG  
ATATTGCCTGGACACACACACACACACACAGCTGCACAGATATGCTGTCTGGACACGCACAC  
ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT  
GCCTGGACACACGCAGATATGCTGTCTAGTCACACACACACGCAGACATGCTGTCCGGACAC  
ACACACGCATGCACAGATATGCTGTCCGGACACACACACGCACGCAGATATGCTGCCTGGAC  
ACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATATTGCCTGGACACACACA  
TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG  
CACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGACACACATGCACACACAGGT  
GCAGATATGCTGCCTGGACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA  
TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA  
TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA  
CACACATGCACACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTGG  
GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT  
CCCTGCTCCACCGTCACTCCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC  
CATCCCCGCTGTGCTCCCTGGCCCTTGGCGGCTATTTTTTGCCACCTGCCTTGGGTGCCAGG  
AGTCCCCTACTGCTGTGGGCTGGGGTTGGGGGCACAGCAGCCCCAAGCCTGAGAGGCTGGAG  
CCCATGGCTAGTGGCTCATCCCCAGTGCATTCTCCCCCTGACACAGAGAAGGGGCCCTTGGTA  
TTTATATTTAAGAAATGAAGATAATATTAATAATGATGGAAGGAAGACTGGGTTCAGGGAC  
TGTGTTCTCTCTGGGGCCCCGGACCCGCTGGTCTTTTCAGCCATGCTGATGCCACACCCC  
GTCCAGGCGACACACCCACCCACCCACTGTGCTGGTGGCCCGAGATCTCTGTAATTTTA  
TGTAGAGTTTGAGCTGAAGCCCCGTATATTTAATTTATTTTGTAAACACAAAA

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**FIGURE 70**

MTPSPLLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM  
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLDLSPGK  
ESLGPDSSSGGQEDPASQQWARPRFTQPSKMRRRVIA RPVGSSVRLKCVASGHPRPDITWMK  
DDQALTRPEAAEPRKKKWTL SLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL  
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD  
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLT VLPDPKPPGPPVASSSSA  
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS  
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTSHHTSHVEGKV  
HQHIHYQC

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**FIGURE 71**

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAACTTCCCAGGGGACCGCATTCCAGAGTC  
AGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCCACGGGCTTGGGGGAAAGATGGTGGGGACCA  
AGGCTTGGGTGTTCTCCTTCCCTGGTCTGGAAGTCACATCTGTGTTGGGGAGACAGACGATGCTCACCCAGTCA  
GTAAGAAGAGTCCAGCCTGGGAAGAAGAACCCAGCATCTTGCCAAGCCTGCCGACACCTGGAGAGCCCTGG  
TGAGTGGACAACATGGTTCAACATCGACTACCCAGGCGGGAAGGGCGACTATGAGCGGCTGGACGCCATTCCGT  
TCTACTATGGGGACCGTGATGTGCCCGTCCCCTGCGGCTAGAGGCTCGGACCACTGACTGGACACCTGCGGGC  
AGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCTCAACAGGGAGCAGCGGCCCTGGCCA  
GAATGCTCTAATTACACCGTACGCTTCTCTGCCACCAAGTCTGCGCCGAGACACAGAGCGCATCTGGA  
GCCCATGGTCTCCCTGGAGCAAGTGCTCAGCTGCCTGTGGTCAGACTGGGGTCCAGACTCGCACACGCTTTGTC  
TTGGCAGAGATGGTGTGCTGTGCACTGAGGCCAGCGAAGAGGGTTCAGCACTGCATGGGCCAGGACTGTACAGC  
CTGTGACCTGACCTGCCAATGGGCCAGGTGAATGCTGACTGTGATGCCTGCATGTGCCAGGACTTCATGCTTC  
ATGGGGCTGTCTCCCTTCCCGGAGGTGCCCGAGCCTCAGGGGCTGCTATCTACCTCCTGACCAAGACGCCGAAG  
CTGCTGACCCAGACAGACAGTGTGGGAGATTCCGAATCCCTGGCTTGTGCCCTGATGGCAAAAGCATCCTGAA  
GATCACAAAGGTCAAGTTTGCCCCATTGTACTCACAAAGCTGCCAAGACTAGCCTGAAGGCAGCCACCATCAAGG  
CAGAGTTTGTGAGGGCAGAGACTCCATACATGGTGATGAACCTGAGACAAAAGCACGGAGAGCTGGGCAGAGC  
GTGTCTCTGTCTGTGAAGGCCACAGGGAAGCCAGGCCAGACAAGTATTTTTGGTATCATAATGACACATTGCT  
GGATCCTTCCCTCTACAAGCATGAGAGCAAGTGGTGGTCTGAGGAACTGCAGCAGCACCAGGCTGGGGAGTACT  
TTTGCAAGGCCAGAGTGATGCTGGGGCTGTGAAGTCCAAGGTTGCCAGCTGATGTGCAGCATCTGATGAG  
ACTCCTTGCAACCCAGTTCCTGAGAGCTATCTTATCCGGCTGCCCATGATTGCTTTCAGATGGCCCAACTC  
CTTCTACTATGACGTGGGACGCTGCCCTGTTAAGACTTGTGACGGGCAGCAGGATAATGGGATGGGCTGGTG  
ATGCTGTGCAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCAGTGGCTACACGCTACCC  
ACCAAGGTGGCCAAGGAGTGCAGTGCAGCGGTGTACGGAAACTCGGAGCATCGTGGGGGGCGGTGTGCTGCTG  
TGCTGACAATGGGGAGCCCATGCGCTTTGGCCATGTGTACATGGGGAACAGCCGTGTAAGCATGACTGGCTACA  
AGGGCACTTTACCCCTCCATGTCCCCAGGACACTGAGAGGCTGGTGTCTACATTTGTGGACAGGCTGCAGAAG  
TTTGTCAACACCAACCAAGTGCTACCTTTCAACAAGAAAGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCG  
TCGGAAGAGGCCCATCACTTTGGAAGCCATGGAGACCAACATCATCCCCCTGGGGGAAGTGGTGGTGAAGACC  
CCATGGCTGAATGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACATAGGAAAAGTGAAG  
GCCAGTGTGACCTTCTGGATCCCGGAATATTTCCACAGCCACAGCTGCCAGACTGACCTGAACCTCATCAA  
TGACGAAGGAGACACTTTCCCCCTTCGGACGTATGGCATGTCTCTGTGGACTTCAGAGATGAGGTACCTCAG  
AGCCACTTAATGCTGGCAAAGTGAAGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACA  
GTGAAACTCTGGTCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAAATTTGAAAATCAAAG  
GAGGAACAAAAGAGAAGACAGAACCTTCTGGTGGGCAACCTGGAGATTCTGTGAGAGGAGGCTCTTTAACTGG  
ATGTTCTGAAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGTGAGAGGTTCTTGCCCTAGTGAGCAG  
ATCCAGGGGGTGTGATCTCCGTGATTAACCTGGAGCTCAACTACCGTCCGACGGACCATGAGGATCCACG  
CCGCTTTGACAGTGTCTACAGGCCCAACGGGGCTGTGTGCTGCTGCTTCTGTGATGACCACTCCCTGATG  
CCTACTCTGCCATGTCTTGGCAAGCCTGGCTGGGGAGGAAGTCAAGCAGTGGAGTCTTCTCTAAATTCAC  
CCAAATGCAATTGGCGTCCCTCAGCCCTATCTCAACAGCTCAACTACCGTCCGACGGACCATGAGGATCCACG  
GGTTAAAAAGACAGCTTTCCAGATTAGCATGGCCAGCCAAAGGCCCAACTCAGCTGAGGAGAGCAATGGGCCCA  
TCTATGCCCTTTGAGAACCTCCGGGCATGTGAAGAGGCCACCCAGTGCAGCCCACTTCCGGTTCTACCAAGATT  
GAGGGGGATCGATATGACTACAACACAGTCCCCTTCAACGAAGATGACCCTATGAGCTGGACTGAAGACTATCT  
GGCATGGTGGCCAAAGCCGATGGAATTCAAGGGCTGTATATCAAGGTGAAGATTGTGGGGCCACTGGAAGTGA  
ATGTGCCGATCCCGCAACATGGGGGGCACTCATCGGCGACAGTGGGGAAGCTGTATGGAATCCGAGATGTGAGG  
AGCACTCGGACAGGGACAGCCCAATGTCTCAGCTGCCTGTCTGGAGTTCAAGTGCAGTGGGATGCTCTATGA  
TCAGGACCGTGTGGACCGCACCCCTGGTGAAGGTATCCCCAGGGCAGCTGCCGTGAGCCAGTGTGAACCCCA  
TGCTGCATGAGTACCTGGTCAACCACTTGCCACTTGCACTCAACAACGACACCACTGAGTACACCATGCTGGCA  
CCCTTGGACCCACTGGGGCCACAATATGGCATCTACACTGTCACTGACCAGGACCCCTCGCACGGCCAAAGGAGAT  
CGCGCTCGGCCGGTGTCTTGTGGCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAGTAGCCC  
TCACCTTCAACTGTGTAGAGAGGCAAGTAGGCCGCCAGAGTGCCTTCCAGTACCTCCAAAGCACCCAGCCAG  
TCCCCTGCTGACGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAGGCGAGCAGCGAGCAGGGGTGGCCAGCG  
CCAGGGTGGAGTGGTGGCCTCTCTGAGATTTCTAGAGTTGCTCAACAGCCCCTGATCAACTAAGTTTTGTGGT  
ACTTACCCCTCTCTGCCCTCATTTCTATGTGACAGCCATTGTGAGACTGATGCACAACTGTCACTTGGTTAAT  
TTAAGCACTTCTGTTTTCTGAATTTGCTTGTGTTTCTTCTATGCCTTTACTTACTTTGTCCCATGCTACTGA  
TTGGCACGTGGCCCCCAATGGCACATAAAGCCCTTTGTGAACTGTTCTTTAAATGAAACACAAGAAAT  
GGCCACTGGTAAACTCTGCAGCTTCAACTGTACTTCAATTAATGCCATTAAATGCAAAATATACTTCTCTTCTT  
TTTGCATGGTTTTGCCCACCTCTGCAATAGTGATAATCTGATGCTGAAGATCAAATAACCAATATAAAGCATAT  
TTCTTGGCCTTGTCCACAGGACATAGGCAAGCCTTGATCATAGTTCATACATATAAATGGTGGTGAATAAAG  
AAATAAAACACAATACTTTTACTTGAAATGTAATAACTTATTTATTTCTTGTCTAAATTTGGAATTTCTAGTGC  
ACATTCAAAGTTAAGCTATTAATATAGGGTGATCATAGTTCCCTCTACCAAGTCTGGAAAGAACATCTCCTGGT  
ATCCACAATTACACAGGTTGCTAAGTGTATTTGCTACATTTCCCTTTGCATTCGCTTTTGTCTTGTCTAGAAAC  
CCAGTGTAGCCAGGGCAGATGTCAATAATGCATACTCTGTATTTGCAAAAAA

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**FIGURE 72**

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESFGEWTTWFNI  
DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSFREGFWCLNREQ  
RPGQNCNYSYTVRFLCPPGSLRRDTERIWSFSPWSPWSKCSAACGQTGVQTRTRICLAEMVSLCS  
EASEEGQHCMGQDCTACDLTCPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAYLLTK  
TPKLLTQTDSDGRFRI PGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPY  
MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRKLQQHQAG  
EYFCKAQSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQATNSFYDVGRCPV  
KTCAGQQDNGIRCDRAVQNCGGISKTEEREIQCSGYTLPTKVAKECSCQRCTETRSIVRGRV  
SAADNGEPMRFGHVYMGNSRVSMGTGYKGTFTLHVPQDTERLVLTFFVDRLQKFVNNTTKVLPFN  
KKGSVAFHEIKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSRSFYRQNGEPIYIGKV  
KASVTFLDPRNISTATAAQTDLNFINDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL  
DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL  
DVPESRRCFVKVRAYRSEFLPSEQIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA  
CVPAFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQPYLNKLNYYRRTDHDPR  
VKKTAFQISMAKPRPNSSAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTVPFN  
EDDPMSWTEDYLAWWPKPMEFRACYIKVKIVGPLEVNVRSRNMGGTHRRVTGKLYGIRDVRS  
TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTLKVI PQGSCRRASVNPMLHEYLVNHLPLAV  
NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTS DGSSRIMKSNVGVALT  
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGRQGGVVASLRFPRVA  
QQPLIN

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**FIGURE 73**

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCCTCAATATACCTGAATACGCAC  
AATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCATCTTCATTTAAAAAAAATACAGAG  
ACCTACCTACCCGTACGCATACATACATATGTGTATATATATGTAACTAGACAAAGATCGCAGATCATAAAGC  
AAGCTCTGCTTGTAGTTTCCAAGAAGATTACAAAGAATTTAGAGATGTATTTGTCAAGATCCCTGTCGATTTCATG  
CCCTTTGGGTTACGGTGTCTCAGTGATGCAGCCCTACCCTTTGGTTTGGGGACATTATGATTTGTGTAAGACT  
CAGATTTACACGGAAGAAGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACATGACAAAATA  
TCTGAAAGTAAAACGATCCTCCGGATATTACCTGTGGAGACCTCCTGAGACGTTCTGTGCAATGGGCAATC  
CCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGAGCTGGCACACCCCCCTGAGCTGATGTTTGATTTT  
GAAGGAAGACATCCCTCCACATTTTGGCAGTCTGCCACTTGGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACAT  
CACTCTGTCTTGGAGCAAAACCATTGAGCTAACAGACAACATAGTTATTACCTTTGAATCTGGGCGTCCAGACC  
AAATGATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAGACTGCTTA  
GATGCTTTTTCATGATGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTCTTAGAAATCATTTGCACAGA  
AGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCACTTTGAAATCAAAGACAGGTTTCGCGCTTTTGT  
CTGGACCTCGCCTACGCAATATGGCTTCCCTCTACGGACAGCTGGATACAACCAAGAACTCAGAGATTTCTTT  
ACAGTCACAGACCTGAGGATAAGGCTGTAAAGACCAGCCGTTGGGGAAATATTTGTAGATGAGCTACACTTGGC  
ACGCTACTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGTAACTCTCCATGCCACTGTATGTG  
TGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACTACAGGTCCAGACTGTGGGAAATGCAAGAAG  
AATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCATCCCCAAAGGCACTGCAAAATACCTGTATCCC  
CAGTATTTCCAGTATTGGTACGAATGTCTGCGACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACA  
ACAACGTGCGCTGCTGTGCCGCGCGCAGACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGCG  
AGCTGCGGCTCCGACTCTGGCCAGGGCGCGCCCCGACGGCACCCCCAGCGCTGCTGCTGCTGACCACGCTGCT  
GGGAACCGCCAGCCCCCTGGTGTCTAGGTTGTACCTCCAGCCACACCGGACGGGCTGTGCCGTGGGGAAGCA  
GACACAACCCAAACATTTGCTACTAATACATAGGAAACACACATACAGACACCCCCACTCAGACAGTGTACAAA  
CTAAGAAGGCCTAACTGAACCTAAGCCATATTTATCACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTT  
TGACTCCAGAGGAGTTGGCAGCTGTTGATATTATCACTGCAAAATCACATTGCCAGCTGCAGAGCATATTGTGGA  
TTGGAAGGCTGCGACAGCCCCCAACAGGAAAGACAAAAACAAACAAATCAACCGACCTAAAAACATTGGC  
TACTCTAGCGTGGTGCGCCCTAGTACGACTCCGCCAGTGTGTGGACCAACCAATAGCATTCTTTGCTGTGAG  
GTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCTGCTTCCGTCCCTGAATCCCTTCCAAC  
CTGTGCTTTAGTGAACGTTGCTCTGTAACCCCTCGTTGGTTGAAAGATTTCTTTGCTGATGTTAGTGATGCACA  
TGTGTAACAGCCCCCTCTAAAAGCGCAAGCCAGTCAACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCGA  
GCACACACCCACTATACAAGAGTGGCTATAGGAAAAAGAAAGTGTATCTATCCTTTTGTATTCAAATGAAGTT  
ATTTTTCTTGAACCTACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGACAATCTGTTAAT  
GTATCTAATTCGAATCAGCAAAGACTGACATTTTATTTGTCTCTTTTCTGTTCTGTTTTGTTTCACTGTGCAGA  
GATTTCTCTGTAAGGGCAACGAACGTGCTGGCATCAAAGAATATCAGTTTACATATATAACAAGTGAATAAGA  
TTCCACCAAAGGACATTCTAAATGTTTTCTTGTGCTTTAACACTGGAAGATTTAAAGAATAAAAACTCCTGCA  
TAAACGATTTTCAAGGAATTTGTATTGCAATTTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTTCACTCACT  
TTACTGATTTCTGTGTGAGTACATTGAGTACGCAATTTAGTTCCAGGAAGATGGATTGATGTTCACT  
AGCTTGGACAACCTTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTACAACAGCAAAAAAAAAAAAAA  
AAAAAA



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**FIGURE 74**

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK  
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK  
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF  
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD  
TTKKLRDFFTVDLRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN  
SKLTCECEHNTTGPDCGKCKKNYQGRPWSPGSYLPIPKGTANTCIPSISSIGTNVCDNELLH  
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS  
PLVF

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**FIGURE 75**

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCGGCTAAGATTGCTGAGGAGGCGG  
CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCGTCCGGGCGAGGTGTCCTCATGACTT  
CTCTTGTGGACC**ATG**TCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC  
CCTCTCAGCCTCTACTGATTTTTTACCACACCCAAGATTTTTTGGAAATGGAGGAGACGGCTCA  
AGAGTTTAGCCTTGCAGCTGGCCCAGTATCCAGGTTCGAGGTTCTGCAGAAGGTTGTGACTTT  
AGTATACATTTTTCTTCTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTC  
AGCAGCCATGGCCTTCTGCTTCTGGAGACCCCTGTGGTGGGAATTCACAGCTTCCTATGACA  
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTCAG  
AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGGAAAAAAT  
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA  
ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA  
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT  
CATTCGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT  
TGGACCAAACCTCG**TG**AGCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT  
CCGGGAGCAGTGATGTCAAACCTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA  
AAAGGGCATGTCAGTGAAATCTGGGAATGGCTGGATTTCGGAAACATCTGCCCATGTGTATTG  
ATGGCAGAGCTGTTGCCACACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT  
TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCTTACATTTATATGATTCTGGGGTT  
GCTTCAGAAGTGTTATTTTCATGAATCATTTCATATGATTTGATCCCCCAGGATTCTATTTTGT  
TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAACCAT  
TTACTTTACATATTCGTTTTCAATACTTGCTGTTTCATGTTACACAAGCTTCTTACGGTTTTTC  
TTGTAACAATAAATATTTTGAAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC  
TAAACTTGTATAAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAATG  
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTTTATTAAAAAAAAAAAAAAAAAAAAA  
AAAAG

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**FIGURE 76**

MSVIFFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFS IHF  
SSF GDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQVKW  
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA  
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

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**FIGURE 77**

TGCTTCCTGGAGACCCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT  
AGCCTCCAGGCCATACGCTTTTCTTGAGTTTGACAGCATCATTGAGAAAGTGAAGTGGCATT  
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAATAATTCAGGAGGAGCTCAAG  
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

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**FIGURE 78**

CTCAGCGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA  
CCCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAAACGAGGCGGGTGCGT  
CCTGCCCTTTAAAGGGCGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT  
TCTGTGCGAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGGCGGCTT  
CCTCCCCGCTCGTCCCTCCCCGGGCCCAGAGGACCTCGGCTTCAGTCATGCTGAGCAGAGTA  
TGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC  
GAGTGTATTATATCAACACTTCTGTTTGAACACTGTACATCCTCTGCCACATCTTCCTGAC  
CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA  
TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCTGCTCCTGCCC  
TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACCTACTACATCCAGTGGCT  
CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTTCTCTTCCCCAACCTGTCCCTCA  
TCTTCCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG  
GGTGTCTGGGCCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT  
AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT  
ATGACTTTTGGGAGTACTATCTCCCCTACCTCTACTCATGCATCTCCTTCCTTGGGGTTCTG  
CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT  
AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG  
CAGCCCTGACCCGCAGGATCTGTAATCCTACTTCCTGCTGGCTGCCTTTAGACATGGAGCTG  
CTACACAGACAGGTCTGGCTCTGCAGACACAGAGGGTCTGCTGGAGAAGAGGCGGAAGGC  
TTCAGCCTGGCAACGGAACCTGGGCTACCCCTGGCTATGCTGTGCTTGCTGGTGCTGACGG  
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG  
CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG  
TGCCGTCAATCAGGTTGTACTCATCTTTTACCTAATGGTGTCTCAGTTGTGGGCTTCTATA  
GCTCTCCACTCTTCCGGAGCCTGCGGCCAGATGGCACGACACTGCCATGACGCAGATAATT  
GGGAACGTGTGTCTGTCTCCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCCTGGG  
GCTCACTCGCTTTGACCTGCTGGGTGACTTTGGACGCTTCAACTGGCTGGGCAATTTCTACA  
TTGTGTTCTCTACAACGCAGCCTTTGCAGGCCTCACCACACTCTGTCTGGTGAAGACCTTC  
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCCTTTGGGCTGGACAGACTGCCGCTGCCCGT  
CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAGTGAACCTCCAGCTGGGGGTGGGA  
AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG  
ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT  
GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAAGTGTGGCCT  
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCTGATCCCAAATCTGTTTACACATCA  
ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTGATGTGCAAT  
AGGGTGGGGTAGGGGCAGGGAAAGGACTGGGCCAGGGCAGGCTCGGGAGATAGATTGTCTCC  
CTTGCCCTTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG  
AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA  
AAAAAA

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**FIGURE 79**

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDATVVK  
IALELCTFTLAIALGAVLLLPFSIISNEVLLSLPRNYIQWLNGSLIHGLWNLVFLFPNLSL  
IFLMPFAYFFTESEGFAGSRKGVLRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL  
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLDLEEQLYCSAFEE  
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRVLLEKRRKASAWQRNLGYPLAMLCLLVLT  
GLSVLIVAIHILELLIDEAAMPGRMGQTSLGQVSFSKLGSGGAVIQVVLIFYLMVSSVVGFY  
SSPLFRSLRPRWHDAMTQIIGNCVCLLVSSALPVFSRTLGLTRFDLLGDFGRFNWLGIFY  
IVFLYNAAFAGLTTLCLVKTFTA AVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ

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**FIGURE 80**

GGCTGCCGAGGGAAGGCCCTTGGGTTGGTCTTGGTTGCTTGGCGGCGGCGGNTTCNTCCCC  
GCTCGTCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC  
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA  
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC  
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG

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**FIGURE 81**

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTTAAACGAGGCGGTGGTGC  
CTGCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTTTC  
TGTCGCAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGTGCTTGGCGGCGGCGGCTTCCT  
CCCCGTTGTCNTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA  
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT  
GTATTATATCAACACTTCTGTTTGCAACACTGTACATCNTCTGCCACATCTTCCTGACCCGC  
TTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGATTGC  
GCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCTCCTGCCCTTCT  
CCATCATCAGCAATGAGGTGCTGCACTCCC



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**FIGURE 82**

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTTGACTGTAAGATCAAGTCCAAACCTGTTTT  
GGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTCATGCTGCTGT  
GGGTGATATTACTGGTCCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGGCCCAT  
ATTTTCCTCCAGCCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCCTCACTTGCAA  
GGGATTTTCGCTTCTACTCACCACAGAAAACAAAATGGTACCATCGGTACCTTGGGAAAGAAA  
TACTAAGAGAAACCCCAGACAATATCCTTGAGGTTTCAGGAATCTGGAGAGTACAGATGCCAG  
GCCCAGGGCTCCCCTCTCAGTAGCCCTGTGCACTTGGATTTTTCTTCAGAGATGGGATTTCC  
TCATGCTGCCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTGCTCACCTTAGGCCTCTC  
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTTCTGTGTTTGAAGGAGAC  
TCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTGAATAATACTATTTACAAGAA  
TGATAATGTCCTGGCATTCCCTTAATAAAAAGAACTGACTTCAAAAAAAAAAAAAAAAAAAAA  
AAA

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**FIGURE 83**

MLLWVILLVLAPVSGQFARTPRPIIFLQPPWTTVFQGERVTLTCKGFRFYSPQKTKWYHRYL  
GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLDFSSEMGFPHAAQANVELLGSSDLLT

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**FIGURE 84**

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCGCGCCCCCGGTGT  
GAGGCGGCCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG  
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACC**ATG**GCTCCGCAGAACCTGAGCACCTTTT  
GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG  
GGGGTGCCTCGAAGTGCCCTCTATAAAGGATATTAAAAAGGCCTATAGGAACTAGCCCTGCA  
GCTTCATCCCGACCGGAACCCTGATGATCCACAAGCCCAGGAGAAATTCAGGATCTGGGTG  
CTGCTTATGAGGTTCTGTGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA  
GGATTAAGAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTCACACTTCTTTGGGGATTT  
TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA  
TTATTGTAGATCTAGAAGTCACCTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT  
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTGCGCAAGAGAT  
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT  
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG  
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG  
AGATTTACGGTTCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT  
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT  
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCCAGGCCAGGAGCGAAGCT  
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA  
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA  
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATAT**TG**AGAGTG  
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT  
TTGTGTGTGTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTATCTAATGA  
TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTCGGAAAAGAATGACC  
AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCTGAGT  
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA  
GTTGTTAGCAATTTCAATTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTTG  
TTATTTTTTA

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**FIGURE 85**

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRASIKDIKKAYRKLALQLHPDRNPDDPQ  
AQEKFQDLGAAYEVLSDSEKRKQYDTYGEGLKDGHQSSHGDI FSHFFGDFGFMFGGT PRQQ  
DRNI PRGSDIIVDLEVTLEEYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ  
MTQEVVCDECPNVKLVNEERTLEVEIEPGVRDGM EY PFIGEGEPHVDGEPGDLRFRIKVVKH  
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVVHISRDKITRPGAKLWKKGEGLPNFD  
NNNIKGSIIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

**Important features:****Signal peptide:**

amino acids 1-22

**Cell attachment sequence.**

amino acids 254-257

**Nt-dnaJ domain signature.**

amino acids 67-87

**Homologous region to Nt-dnaJ domain proteins.**

amino acids 26-58

**N-glycosylation site.**

amino acids 5-9, 261-265

**Tyrosine kinase phosphorylation site.**

amino acids 253-260

**N-myristoylation site.**

amino acids 18-24, 31-37, 93-99, 215-221

**Amidation site.**

amino acids 164-168

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**FIGURE 86**

TGGGACCAGGGAACCCCGGGCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA  
GCGGCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT  
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG  
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAGGATATTA AAAAGG  
CCTATAGGAACTAGCCCTGCAGNTTTATCCCGACCGGAACCCTGATGATCCACAAGCCCAG  
GAGAAATTCCAGGATTTGGGTGCTGCTTATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA  
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT  
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA  
AATATTCCAAGAG

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**FIGURE 87**

GGCACGAGGCGGCGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT  
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA  
GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGC**ATGG**  
AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGCAGCC  
TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGGCCGCGAGACCTGCTGCAGCGCTATGATTG  
TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC  
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC  
GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACACTCTGAC  
AGAGAAGCTTGTTGCCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA  
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG  
TACCCTCCGTTGGACCCCAAACCTCCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGTCAG  
TCACCTGGTGCTGGTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC  
AGTCTCTGTCGGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG  
CCAGATAAAGGCCCTCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATTT**TAGT**GCCT  
ACAGGCCAGCAGCTAGCCATGAAGGCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT  
CTACTTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGTGCATAG  
TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACTGTGGCTGGTGAGT  
GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA  
CTGGTGGACTGTCAGCTTTATTTAGCTCACCTAGTGTTTTCAAGAAAATTGAGCCACCGTCT  
AAGAAATCAAGAGGTTTCACATTAATAATTAGAATTTCTGGCCTCTCTCGATCGGTCAGAATG  
TGTGGCAATTCTGATCTGCATTTTTCAGAAGAGGACAATCAATTGAAACTAAGTAGGGGTTTC  
TTCTTTTGGCAAGACTTGTA CTCTCACCTGGCCTGTTTCATTTATTTGTATTATCTGCCT  
GGTCCCTGAGGCGTCTGGGTCTCTCCTCTCCCTTGCAAGTTTGGGTTTGAAGCTGAGGAACT  
ACAAAGTTGATGATTTCTTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG  
GATAGTAAATTTATACTTATGTTTCCCTCAAAAAAAAAAAAAA

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**FIGURE 88**

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSSEL  
ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTLTEKLVAMTMGSGAKMKSAS  
VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLSVSHLVLVTRNACHLTGGLDWI  
DQSLSAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

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**FIGURE 89**

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTCCGAGGTGCTTTCGCCGCTGTCC  
CCACCACTGCAGCCATGATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA  
TTTGGAGTGTTTTTCCTGTTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT  
TGAAATGTTTTATTTGTAGCCGGCTTGGCTTTTGTAATTGGTTTAGAAAGAACATTTCAGAT  
TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTC  
CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTTCTCTTGTTTCAG  
GGGCTTCTTTCCTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT  
TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTATTAACAACA  
AGTGAATTTGAAGACTCATTTAAAATATTGTGTTATTTATAAAGTCATTTGAAGAATATTCA  
GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG  
CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA  
ACTAAGAAGAAGTCAGCAAGCAAAGTGAAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA  
ACTCTTGAAGGCTATTTGTGTTGTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA  
CTGTGGTGCCTGTTTCTTTTCTTTTATTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT  
TTTTAGAAGTGTCCTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA  
TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTTAAACCAAGGAAACCCCAATTTTG  
ATGTATGGATTACTTTTTTTTGNGCNCAGGGCC



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**FIGURE 90**

MISLTDQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK  
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFIIRVPVLGSLNLPGI  
RSFVDKVGESNNMV

**Important features:**

**Transmembrane domains:**

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

**N-myristoylation sites.**

amino acids 11-16, 51-56 and 116-121

**Aminoacyl-transfer RNA synthetases class-II protein.**

amino acids 49-59

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**FIGURE 91**

GAAGACGTGGCGGCTCTCGCCTGGGCTGTTTCCCGGCTTCATTTCTCCCGACTCAGCTTCCC  
ACCNTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCCCCACCACTGCAGCCATGATCTCCTTAA  
CGGACACGCAGAAAATTGGAATGGGATTAACCGGATTTGGAGTGTTTTTCCTGTTCTTTGGA  
ATGATTCTCTTTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTTATTTGTAGCCGGCTT  
GGCTTTTGTAATTGGTTTAGAAAGAACATTTCAGATTCTTCTTCCAAAACATAAAATGAAAG  
CTACAGGTTTTTTTCTGGGTGGTGTATTTGTAGTCCTTATTGGTTGGCCTTTGATAGGCATG  
ATCTTCGAAATTTATGGATTTTTTCTCTTGTTT

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**FIGURE 92**

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA  
GGCTGCCAGGAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCTTCTGGAAATCTTTGA  
CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC  
TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC  
ATCAACACCATTTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA  
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT  
CGGGCACGGAATGCACCATCTTCACGGACCCGCGCGCCTACCTCAAGTATGGGAAGGAAAAT  
GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA  
ACGCTTTGGGCTGTTAGGGGGCTCCAAGGTCCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA  
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTTCGCGCAAGTGGGAGCAGGAT  
CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCTCT  
GATTCAGTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC  
GGGCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC  
ACCGTGAGGAGCTTGAGAAATGTAGTTTCAGCTGTATATGACTGTACACTCAATTTTCAGAAA  
TAATGAAAATCCAACACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATG  
TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC  
AAGCTCTACCAGGAGAAGGATGCCTTTTCAGGAGGAGTACTACAGGACGGGCACCTTCCCAGA  
GACGCCCATGGTGCCCCCCCCGGCGGCCCTGGACCCTCGTGAAGTGGCTGTTTTGGGCCCTCGC  
TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG  
CTGGCCAGCTTCATCCTCGTCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGT  
GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAAGCAGAACTGAATGACT  
GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT  
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCTGCTGGGCACGGCGGAAGTCACGA  
CCTCTCCAGCCAGGGAGTCTGGTCTCAAGGCCGGATGGGGAGGAAGATGTTTTGTAATCTTT  
TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTGTGCGAGTGTGTGTGAGAAATGGC  
TGTGTGGTGAGTGTGAACTTTGTTCTGTGATCATAGAAAGGGTATTTTAGGCTGCAGGGGAG  
GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCCCTTTCATCCTTTGGTGCTGAGTTTTCTGT  
AACCCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC  
CAAGAAAAAAAATTAAAGTGCTTTTCTGGGTCAAAAAAAAAAAAA

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**FIGURE 93**

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLWPINKQLFRKINCRLSYCISSQLV  
MLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHNKFEIDFLCGWSLSERFGLLGSKVLAKK  
ELAYVPIIGWMWYFTEMVFCSRKWEQDRKT VATSLQHLDYPEKYFFLIHCEGTRFTEKKHE  
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVLNGKK  
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQEKDAFQEEYYRTGTFPETPMVPPRRPWTLVN  
WLFWASLVLYPFFQFLVSMIRSGSSLTASFILVFFVASVGVRWMIGVTEIDKGSAYGNSDS  
KQKLND

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**FIGURE 94**

CTGAGGCGGCGGTAGCATGGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG  
GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA  
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA  
TACAATTGACATTCAGAAATATATTCCATGCTATCAGCTTTTTAGCTTTTATAATTCTTCAG  
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT  
TGGTACAAATTCCGTCGTCATTGATCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAA  
AACTTGCGAGGAGCATTTTTTCAAACCAAGACCTTGTTTTCTGCTATTAACACCAAGTATAA  
TAACAGAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT  
TTTCACAGGGTACCTTTAGTGGTTGCCAATCTGGGCATGTCTGAACAACCTGGGTTATAAAAC  
TGTATCAGGTTCCCTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT  
TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA  
CAAGAGGAATTAAAGAGTATATGCAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT  
AGTAAAGGATGTAAACAGATTAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG  
CAGCAAGAGAGAAGAACATCCAAAAGACCCTCAGGAGAACATTTTTCTTTGTCAGGCATTA  
CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTTCATGTGTTATGTCTTTAAAAAATAGACA  
TGTTTCTAAAAGTAGCTGTAACACACCACCATCTCGATGTAGTAGACAATCTGACCTTAA  
TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCAT  
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAGAGATCTCGGTTGTTAGATACACAAGA  
CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAATGAGCAGCC  
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA  
TTTTTGATCCTTTTAAACCTTACAAGGAGATTTTTTTATTTGGCTGATGGGTAAAGCCAAACAT  
TTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTTAC  
CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTCAAAC  
ATCAGATGCTTTTATTTCCAAACCTTTTTTTCACCTTTCCTAAGTTGTTGAGGGGAAGGCT  
TACACAGACACATTCCTTTAGAATTGGAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA  
TCCCAGCACTTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC  
TGGGCAACGTATTGAGACCATGTCTATTAAAAAATAAAATGGAAAAGCAAGAATAGCCTTAT  
TTTCAAATATGGAAGAAATTTATATGAAAATTTATCTGAGTCATTAAAATTCTCCTTAAG  
TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA  
ATAAATTTGCAAAACATCATCTAAAATTTAAAAAATAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 95**

MEGESTSAVLSGFVLGALAFQHLNTDSDTEGFLLGGEVKGAKNSITDSQMDDVEVVYTIIDIQ  
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH  
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC  
MSTGFSRAVQTHSSKFFEEEDGSLKEVHKINEMYASLQEELKSICKKVEDSEQAVDKLVKDVN  
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS  
CNYNHHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDDDRWFQKRSRLLDTDQKRSKA  
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTF

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**FIGURE 96**

GGCACAGCCGCGCGGCGGAGGGCAGAGTCAAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCAGCGCAGGGCAGC  
CCAAGCAGCGCGCAGCGAACGCCCCGCCGCCGCCACACCCCTCTGCGGTCCCCGCGGCGCCTGCCACCCCTCCCT  
CCTTCCCCGCGTCCCCGCGCTCGCCGGCCAGTCAGCTTGCCGGGTTCGCTGCCCCGCGAAACCCCGAGGTACCA  
GCCCCGCGCTCTGCTTCCCTGGGCGCGCGCGCCCTCCACGCCCTCCTTCTCCCTGGCCCGGCGCCTGGCACCC  
GGGGACCGTTGCTGACGCGAGGCCAGCTCTACTTTTCGCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCAC  
CAACTCCAACCTCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCCCGCTGCCGTAG  
CGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCGGCCCGCACCAATGGCACGGTTTCGGCTTGCC  
CGCGCTTCTCTGCACCCCTGGCAGTGCTCAGCGCCGCGCTGCTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGG  
AAGTGCGACGTCTTTACGTGTCCAAAGGCTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCAT  
TTGAAGATCTGTCCCCAGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGA  
TGATTTCAAAGTGTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTACGTTACAAGAAGTTTG  
ATGAATTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGTTTGTGAAGACATATGGCCAT  
TTATACATGCAAATTTCTGAGCTATTTAAAGATCTCTTCGTAGAGTTGAAACGTTACTACGTGGTGGGAAATGT  
GAACCTGGAAGAAATGCTAAATGACTTCTGGGCTCGCCTCCTGGAGCGGATGTTCCGCTGGTGAACCTCCAGT  
ACCACTTTACAGATGAGTATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCT  
CGCAAATTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTGCTCAAGGCTTAGCGGTTGCGGG  
AGATGTCGTGAGCAAGGTCTCCGTGGTAAACCCACAGCCAGTGTACCCATGCCCTGTTGAAGATGATCTACT  
GCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAACCTACTGCTCAAACATCATGAGAGGCTGTTG  
GCCAACCAAGGGGATCTCGATTTTGAATGGAACAATTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGA  
GGGTCTTTTCAACATTGAATCGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGG  
ATAATAGTGTTCAAGTGCTCAGAAGGTTTTCCAGGGATGTGGACCCCCAAGCCCTCCAGCTGGACGAATT  
TCTCGTTCCATCTCTGAAAGTGCCTTCAGTGCTCGCTTCAGACCACATCACCCCGAGGAACGCCCCAACACAGC  
AGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAACTGAAACAGGCCAAGAAATCTGGTCTCT  
CCCTTCCGAGCAACGTTTGCAACGATGAGAGGATGGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGG  
AAAGGCAAAAGCAGGTACCTGTTTGCAGTGACAGGAAATGGATTAGCCAACAGGGCAACAACCCAGAGGTCCA  
GGTTGACACCAGCAAACCAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGATGA  
AGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAGAAGGAAGTGAAGT  
GGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTACTACAAATGCCACTGACCATGCTGGGAAGAGTGCCAAATGA  
GAAAGCCGACAGTGCTGGTGTCCGTCTGGGGCACAGGCCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGG  
TTATGCAGAGAGAGTGGAGATAATTCTCAAACCTCTGAGAAAAAGTGTTTCATCAAAAAGTTAAAGGCACCAAGT  
ATCACTTTTCTACCATCCTAGTGACTTTGCTTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC  
CACTGGTTTTAAGAAGTGCTGACTTTGTTTTCTCATTCAGTTTTGGGAGGAAAAGGGACTGTGCATTGAGTTGGT  
TCCTGCTCCCCAAACCATGTTAAACGTGGCTAACAGTGTAGGTACAGAACTATAGTTAGTTGTGCATTTGTGA  
TTTTATCACTCTATTATTTGTTTGTATGTTTTTTTCTCATTTCGTTTGTGGGTTTTTTTTTCCAACGTGTGATCT  
CGCCTTGTTTCTTACAAGCAAACCAGGGTCCCTTCTTGGCAGTAACATGTACGTATTTCTGAAATATTAAATA  
GCTGTACAGAAGCAGGTTTTATTATCATGTTATCTTATTAAGAAAAAGCCCAAAAGC

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**FIGURE 97**

MARFGLPALLCTLAVLSAALLAAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ  
GSTCCSQEMEKEYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSLNDMF  
VKTYGHLYMQNSELFKDLFVELKRYVVGVNLEEMLNDFWARLLERMFLVNSQYHFTDEY  
LECVSKYTEQLKPFQDVPRKLLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL  
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLDFEWNNFIDAMLMVAERLEGPFNIES  
VMDPIDVKISDAIMNQDNSVQVSQKVFQGCQPPKPLPAGRISRSISESAFSARFRPHHPEE  
RPTTAAGTSLDRLVTDVKEKLQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYL  
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFDISDESSGE  
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR



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**FIGURE 98**

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCT  
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAA  
GCAACTTACAGCTGCACCGACAGTTGCGATGAAAGTTCTAATCTCTTCCCTCCTCCTGTTGC  
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCAC  
AGGGACCGAGGCCAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAA  
AGATTGGTTCCTGAGAGCCCCGAGAAGAAAATTCATGACAGTGTCTGGGCTGCCAAAGAAGC  
AGTGCCCCTGTGATCATTTCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCACAGA  
AAGCCAAACAAGCATTCCAGAGCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTT  
TGCTCTGCCTTTGTAGGAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA  
GACAGTGAGCACACCTACCAGACACTCTTCTTCTCCACCTCACTCTCCCACTGTACCCACC  
CCTAAATCATTCCAGTGCTCTCAAAAAGCATGTTTTTCAAGATCATTTTGTTTGTTGCTCTC  
TCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCCTTACCCAGGCTTAGGCTT  
AATTACCTGAAAGATTCCAGGAAACTGTAGCTTCCTAGCTAGTGTCAATTAACCTTAAATGC  
AATCAGGAAAGTAGCAAACAGAAGTCAATAAATATTTTAAATGTCAAAAAAAAAAAAAAAAAA

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**FIGURE 99**

MKVLISLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR  
KFMTVSGLPKKQCPDHFKNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

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**FIGURE 100**

**AAT**GGCTGTCTTAGTACTTCGCCTGACAGTTGTCCTGGGACTGCTTGTCTTATTCCTGACCT  
GCTATGCAGACGACAAACCAGACAAGCCAGACGACAAGCCAGACGACTCGGGCAAAGACCCA  
AAGCCAGACTTCCCCAAATTCCTAAGCCTCCTGGGCACAGAGATCATTGAGAATGCAGTCGA  
GTTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTTATGGAATTTGATGATAATGAAGGAA  
AACATTCATCAAAG**TGAC**ATCCTCAGGACACACCCATGTGGCTCCTGGACAATCCAAGAGCA  
GCCAAATCCTGCTTTTCCAGTTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTCAAAGCAAC  
TCCCAACGAGTTCTCAGGATTCAGGCTCTGGCTTCAACCAAACAGAACTCATTTTGAACACC  
CTGACTGCATTTTTGCTTTTAGAAAGTTAGAATAAATATGGCGCTTTGGGATCACATAGTTG  
ATGGAGAGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 101**

MAVLVLRLTVVLGLLVLFLTCYADDKPKDPDDKPDGKDPKPDFPKFLSLLGTEIIENAVE  
FILRSMSRSTGFMEFDDNEGKHSSK

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**FIGURE 102**

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT  
CAGAGCTGGTCTGCCATGGACATCCTGGTCCCCTCCTGCAGCTGCTGGTGCTGCTTCTTAC  
CCTGCCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCCTGTGAAAAGCTACTTCC  
CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG  
CTCTTCAGCCAGATAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG  
CTGCGGAACCGGAGCCAACTTTTCACTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC  
CAAATCCCCACTTTTGAAGAAGTTTCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT  
GAGCGGTTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT  
GGTGGTCTGCACTCTGGTGCTGTGCTCTGTGCAGAGCCCCAAGGAAGGTCTTGCAGGAGGTCC  
GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA  
AGCTGGGCCTTCATGTGGCAGCAAGTTTTTCGAGCCCCACCTGGAAACACATTGGGATGGCTG  
CTGCCTCACCAGAGAGACCTGGAAGGATCTTGAGAACGCCAGTTCTCCGAAATCCAAATGG  
AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC  
AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA  
AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCTAGCAGAATGAGAGAAGACATT  
CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC  
CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC  
TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC  
CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT  
CTCTAGGAAGTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCTCT  
CTCCCCACTACCACCTTCTTCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT  
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTTCTCAAATATTTTTTAATAAATAGACGA  
AACCACG

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**FIGURE 103**

MDILVPLLQLLVLLLTLPPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELF SQI  
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVV  
APGEDMRQLADGSMDVVVCTLVLCVQS PRKVLQEVRRLRPGGVLFFWEHVAEPYGSWAFM  
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPVGPHIMGKAVKQSFP  
SSKALICSFPSLQLEQATHQPIYLPLRGT

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**FIGURE 104**

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGAAGTTGCCTCATCGCAGG  
CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA  
ACTAATATTTATATGACAGAAGAAAAAGATGTCATTCCGTAAAGTAAACATCATCATCTTGG  
TCCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTG  
TTAAGGAATGAGGTTACAGATTCAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAA  
TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATCTG  
AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTTCAGCACAACTCGCTCCAAT  
GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAG  
TGATTCCCTGAAAAGCATCAGATACAAAATTGTCAATTTTGACCCTAACTTTTGGAAGGAA  
AAGTAAAGGAGGATCCTGACCAGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC  
TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA  
AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG  
AAGATTGTGATTCAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC  
ATTGGCTATCTTGACTATAAAAAGGAAAGAATTTCGTAAGCTTTCCATGAAAGCCAGCACTTG  
CTCATTTAATCCTGGAGTTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA  
ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCTGGCT  
GGTAGCATCACAAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC  
TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTAA  
AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT  
ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTCAACCTAATCCGAAG  
ATATACCGAGATCTCAAACATAAAGTGAAACAGAATTTGAACTGTAAGCAAGCATTTCTCAG  
GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA  
GCAAGCCATGGAAAAAGATGTGTCAGCTAGGTAAAGATGACAACTGCCCTGTCTGGCAGTC  
AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTTTTCTT  
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTTCAGCTAGCTGGTACAGA  
TAATTCAAACCTGCTGTTGGTTTTAATTTTGTAACTGTGGCCTGATCTGTAAATAAACTT  
ACATTTTTC

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**FIGURE 105**

MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLLRNEVTD SGIVGPQPIDFVPNALRHAVDGR  
QEEIPVVIAASEDRLGGAIAAINSIQHNTSRNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK  
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT  
ALKPGHAAAFSEDCDSASTKVVIRGAGNQYNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA  
NLTEWKQRQITNQLEKWMKLNVEEGLYSRTLGSITTPPLLIVFYQQHSTIDPMWNVRHLGS  
SAGKRYSPQFVKAALLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK



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**FIGURE 106**

TGGTTTTTGCCCCATAAATTCCTCAGCTTGAGCAGTTTGTTAAGGAATGAGGTTACAGATT  
CAGGAATTNTAGGNCCTCAACCTNTAGANTTTGTCCCAAATGTTCTCCGACATGCAGTAGAT  
GGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATNTGAAGACAGGCTTGGGGGGGCCAT  
TGCAGCTATAAACAGCATTTCAGCACAACACTCGNTCCAATGTGATTTTCTACATTGTTACTC  
TCAACAATACAGCAGACCATNTCCGGTCCTGGNTCAACAGTGATTCCTGAAAAGCATCAGA  
TACAAAATTGTCAATTTTGACCCTAACTTTTGGAAGGAAAAGTAAAGGAGGATCCTGACCA  
GGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGTTCCCAGCG  
CAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTAC  
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTAC  
TAAAGTTGTCATCCGTGGAGCAGGAAA

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**FIGURE 107**

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCTGGGCGTAGTGGGGCTGCGCGGCTGCCACG  
GAGCTAGAGGGCAAGTGTGCTCGGCCAGCGTGCAGGGAACGCGGGCGGCCAGACAACGGGC  
TGGGCTCCGGGGCCTGCGGCGCGGGCGCTGAGCTGGCAGGGCGGGTCGGGGCGCGGGCTGCA  
TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT  
TGTCGGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGGAGCGTCACATCACT  
TTCCGATCACTTCAAAGTGGTTAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT  
CCGTAAAGTAAACATCATCATCTTGGTCTGGGCTGTTGCTCTCTTCTTACTGGTTTTGCAC  
CATAACTTCCTCAGCTTGAGGCAGTTTGTTAAGGAATGAGGTTACAGATTCAGGAATTGTAG  
GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA  
GGAGATTCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA  
ACAGCATTTCAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA  
GCAGACCATCTCCGGTCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG  
TCAATTTTGACCCTAACTTTTGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGAATCC  
ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCCAGCGCAAAGAAGG  
CCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA  
CTGAAGCCAGGACATGCAGCTGCATTTTTCAGAAGATTGTGATTCAGCCTCTACTAAAGTTGT  
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA  
TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTGCAAAC  
CTGACGGAATGGAAACGACAGAATATACTAACCAACTGGAAAAATGGATGAACTCAATGT  
AGAAGAGGGACTGTATAGCAGAACCCTGGCTGGTAGCATCACAACACCTCCTCTGCTTATCG  
TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGTTCCAGT  
GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA  
TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA  
GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA  
CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG  
TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG  
GTAAAGATGACAACTGCCCTGTCTGGCAGTCAGCTTCCCAGACAGACTATAGACTATAAAT  
ATGTCTCCATCTGCCTTACCAAGTGTTCCTTACTACAATGCTGAATGACTGGAAAGAAGAA  
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAACCTGCTGTTGGTTTTAATTTT  
GTAACCTGTGGCCTGATCTGTAAATAAACTTACATTTTTCAATAGGTAAAAA

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**FIGURE 108**

CTGCAGGTAGACATCTCCACTGCCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT  
GAAGGCCGCGCCATACCAGAGTCCTGCCTCGGCATGGGCCTCACCATTGAGGCAGCTCCACTG  
TCTGTGCTGGTCTGAGGGTGCTGCCTGTCATGGGGGCAGCCATCTCCCAGGGGGCCCTCATC  
GCCATCGTCTGCAACGGTCTCGTGGGCTTCTTGCTGCTGCTGCTCTGGGTCATCCTCTGCTG  
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTCTGAATCCAGTCCCAACTCCAGCCC  
TGGCCCCCTGTCCTGAGAAGGCCCCACCACCCCAGAAGCCCAGCCATGAAGGCAGCTACCTGC  
TGCAGCCCTGAAGGCCCTGGCCTAGCCTGGAGCCCAGGACCTAAGTCCACCTCACCTAGAG  
CCTGGAATTAGGATCCCAGAGTTCAGCCAGCCTGGGGTCCAGAACTCAAGAGTCCGCCTGCT  
TGGAGCTGGACCCAGCGGCCAGAGTCTAGCCAGCTTGGCTCCAATAGGAGCTCAGTGGCCC  
TAAGGAGATGGGCCTGGGGTGGGGGCTTATGAGTTGGTGCTAGAGCCAGGGCCATCTGGACT  
ATGCTCCATCCCAAGGGCCAAGGGTCAGGGGCGGGTCCACTCTTTCCTAGGCTGAGCACC  
TCTAGGCCCTCTAGGTTGGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG  
GCTGGGCCCCCTCCCCTGGTCCTCCCAGTGTTTGCTGGATAATAAATGGAACCTATGGCTCTAA  
AAAAAAAAAAAAAAAAAAAA

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**FIGURE 109**

MGAASQGALIAIVCNGLVGFLLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRPHH  
PRSPAMKAATCCSPEGPWPSLEPRT

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**FIGURE 110**

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA  
GTTCCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA  
CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGAA  
TC**ATG**TCGGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC  
ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTTCATTGGTTAT  
TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC  
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCGTGCTGGGGTTTGCTATCGTA  
TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT  
GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC  
AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCTCTGGGTGGCTGTGCTGCTG  
AGCCTGGGAACTGCAGGAGCTGCCCAGGTTATGGAAGGCGGCCAAGTGGAATATAAGCCCCCT  
TTCGGGCATTCGGTACATGTGGTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA  
TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT  
AAAAATGATCCTCCTGATCATCCCATCCTTTCGTCTCTCTCCATTCTCTTCTTCTACCATCA  
AGGAACCGTTGTGAAAGGGTCATTTTTAATCTCTGTGGTGAGGATTCCGAGAATCATTGTCA  
TGTACATGCAAACGCACTGAAAGAACAGCAGCATGGTGATTGTCCAGGTACCTGTTCCGA  
TGCTGCTACTGCTGTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA  
TACTACAACCTGCTATTAATGGGACAGATTTCTGTACATCAGCAAAGATGCATTCAAATCT  
TGTCCAAGAACTCAAGTCACTTTACATCTATTAAGTCTTTGGAGACTTCATAATTTTTCTA  
GGAAAGGTGTTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG  
GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCCTACTTAGTAGCCC  
ATAGTTTTTTATCTGTGTTTGAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTGAT  
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT  
CGTAAAAGGAGCAACAAATTAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA  
ATGAGGAGGGGAACAGAACTCCAGGCCATTGTGAGAT**TAG**ATACCCATTAGGTATCTGTACCT  
GGAAAACATTTCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT  
AGTGAATTTTTTTTTTAAAAGACCTAATAAACCCCTATTCTTCCTCAAAA

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**FIGURE 111**

MSGRDTILGLCILALALSLAMMFTFRFITLLVHIFISLVILGLLFVCGVLWWLYDYDTNDL  
SIELDTERENMKCVLGFAIVSTGITAVLLVLI FVLRKRIKLTVELFQITNKAISSAPFLLFQ  
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI  
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM  
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL  
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH  
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN  
EEGTELQAIVR

**FIGURE 112**

[illegible]

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**FIGURE 113**

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC  
PAGCQDPKYHVGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL  
SLPRWRESFIVLESKPKKGVITYPSALTYSSSSKSPAAQAGETTKAYQRPPIPGTTAQPVTLMO  
LLAVTVAVATPTTLPRPSPSAASTTSIPRPQSVGHRSEQEMDLWSTATYTTSSQNRPRADPGIQ  
RQDPGAAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR  
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHTNRDLKTAIEKITQRGGLSNV  
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE  
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLOPLVKRVCDTDRACSKTCLNSADI  
GFVIDGSSSVGTGNFRTVLQFVTNLTKFEISDTRIGAVQYTYEQRLEFGFDKYSSKPD  
LNAIKRVGYWSSGTSTGAAINFALEQLFKKSKPNKRKLMILITDGRSYDDVRI PAMAAHLKG  
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFNLHQYVPRIIQNICTEFNSQPRN



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**FIGURE 114**

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA  
**TG**CCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT  
GCGCCAGGTCCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT  
TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG  
TGCTCCAGGACAGCGTGGACTTTGATATTGATGTGAACGCCTCTGTGTTTGAAACAAACATT  
CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA  
GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAATGGCTGAGGAGGCGGCCCCGAAAACCTCC  
TCCCAGCCTTTCAGACCCCCACTGGCATGCCATATGGAACAGTGAACTTACTTCATGGCGTG  
AACCCAGGAGAGACCCCTGTACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC  
CACCTTGAGCAGCCTCACTGGTGACCCGGTGTTTGAAGATGTGGCCAGAGTGGCTTTGATGC  
GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC  
AAGTGGGTGGCCAGGACGCAGGCATCGGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT  
GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCTAGAGTATAACAAAG  
CCATCCGGAACACACCCGCTTCGATGACTGGTACCTGTGGGTTTCAGATGTACAAGGGGACT  
GTGTCCATGCCAGTCTTCCAGTCCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG  
AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG  
GGCTCCCGGAATTCTACAACATTCTCAGGGATACACAGTGGAGAAGCGAGAGGGGCTACCCA  
CTTCGGCCAGAATTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCT  
CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGC GGAT  
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG  
GCCGAGACTGTGAAATACCTCTACCTCCTGTTTGACCCAACCAACTTCATCCACAACAATGG  
GTCCACCTTCGACGCGGTGATCACCCCTATGGGGAGTGCATCCTGGGGGCTGGGGGGTACA  
TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG  
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC  
GAAATTTTCAGAAAAACACTGTTAGTTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC  
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCCA  
CTTCTCAGCTGCCCCAGTCAGCCCTTACCTCCAAGTTGGCATTACTGGGACAGGTTTTCT  
AGACTCCTCA**TAA**CCACTGGATAATTTTTTTATTTTTATTTTTTTGAGGCTAAACTATAATA  
AATTGCTTTTGGCTATCATAAAA

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**FIGURE 115**

MPFRLLIPLGLLCALLPQHGGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE  
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLLSKKAGVEVEAGWPCSGPLLMAEEAARKL  
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM  
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK  
AIRNYTRFDDWYLVVQMYKGTVMFVQSLEAYWPGQLQSLIGDIDNAMRTFLNYYTVWKQFG  
GLPEFYNIPOGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG  
FATIKDLRDHKLDRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY  
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT  
LFSPENHDQARERKPAKQKVPLLSCPSQPFTSKLALLGQVFLDSS

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**FIGURE 116**

AAAGTTACATTTTCTCTGGAACCTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG  
GGCAGAAAGGAGGGTGCTTCGGAGCCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA  
ATTCAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT  
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACCTGAGTCTACCA  
AATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCT  
ACGCATTGATTCCATGTTTGCTCACAGATGAAAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC  
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA  
AACAGTGTACTATTCTGTGCAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT  
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC  
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG  
GAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTACCCGACCTGGGATGGAGA  
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC  
CTTGTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG  
GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA  
CATTTCGTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA  
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCCTTTGTTGGCTTCATGCTGATCCTTGT  
GGTCGTGCCACTGTTTCGTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG  
TGGTCCCTCCCAGACACCTTGAAAATAACCAATTACCCCAGAAGTTAATCAGCTGCAGAAGG  
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT  
CTCATAGGTTTGCGGAAGGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC  
ATGAGGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA  
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC  
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC  
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC  
TACACACCTGCTAAACACACACACACAGAGTCTCTCTATATATACACACGTACACATAAA  
TACACCCAGCACTTGCAAGGCTAGAGGGAACTGGTGACACTCTACAGTCTGACTGATTAG  
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT  
GGCTTGGAGAGCCCACTTTCCCAGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG  
TGTTGAGTTCACTTCAAGCCCAATGCCGGTGAGAGGGGAATGGCTTAGCGAGCTCTACAGT  
AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC  
CATGAATACTGTAAAGTGTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT  
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC  
TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA  
AAAAA

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## **FIGURE 117**

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLMLWSPVIAPGE  
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTS  
SILKHPFNRNSTILTRPGMEITKDGFLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG  
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMILILV  
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

**Important features:**

**Signal peptide:**

amino acids 1-29

**Transmembrane domain:**

amino acids 230-255

**N-glycosylation sites.**

amino acids 40-43 and 134-137

**Tissue factor proteins homology.**

amino acids 92-119

**Integrins alpha chain protein homology.**

amino acids 232-262

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**FIGURE 118**

TCCTGCTGATGCACATCTGGGTTTGGCAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT  
CCTGGCCGGCTCTAGAACAATTCAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA  
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGAAAGAAACAATGTTCTAGG  
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT  
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC  
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA  
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTCTGAATACCAGGGGGAGTACGAGAGCCT  
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG  
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTGAGGGCCACATTGGGC  
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTAC  
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG  
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG  
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCCAC  
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTTGAT

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**FIGURE 119**

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGGCGTG  
GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG  
TCAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG  
AATGTGGCCAGCGAGTGCGGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG  
AGACCTGGGCCCCCACCACCTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG  
AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCCGCGCACCTACAGTGTCTCATTCCCC  
ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA  
GACTTCTGGGAAGGAGCCCACCTGGAACCTTCTGGAAGTACCTAGTAGCCCCAGATGGAAAGG  
TGGTAGGGGCTTGGGACCCAACTGTGTCAGTGGAGGAGGTGAGACCCAGATCACAGCGCTC  
GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTATTAACCACCGCGTCTCCTCCTCCACCA  
CCTCATCCCCGCCACCTGTGTGGGGCTGACCAATGCAAACTCAAATGGTGCTTCAAAGGGAG  
AGACCCACTGACTCTCCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA  
AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG  
AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAAA  
TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAACTGGGACCAATGATTAC  
CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC  
CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATAACTTGTTATCAAT  
AAAACTTGCATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT  
GTTATTTCTCTGTATTATTTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA  
ACAATACCTCACGATATAAAATAAAAATGAAAGTATCCTCCTCAAAA

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**FIGURE 120**

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLVKYRGSVSLVVNVASECGFTDQ  
HYRALQQLQRD LGPHHFNVLA FPCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG  
AHPAFKYLAQTSGKEPTWNFWKYL VAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

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**FIGURE 121**

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCC**ATGG**GCTGTCTACGTCGGGATGC  
TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGCCCCGGGCCGCCCTCTCT  
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG  
CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTCAAGGGGTGCACCAAAAAGCATCTTA  
ACAGCAAGACTGTGGGCCAGTGCCTGGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGCC  
TTGGTCGTCCTCCATGAAGACGTCAAGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA  
AGCTGCTTCTGGCCTCCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGGCATGTGGGGAC  
CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCAGGCGGGCATCATTCTGGTG  
TCTGTGAACCCAGCCTACCAGGCTATGGAAGTGGAGTATGTCTCAAGAAGGTGGGCTGCAA  
GGCCCTTGTTGTTCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCTCTGAAGCAGATCT  
GTCCAGAAGTGGAGAAATGCCAGCCAGGGGCTTGAAAGAGTCAGAGGCTCCCAGATCTGACC  
ACAGTCATCTCGGTGGATGCCCTTTGCCGGGGACCCTGCTCCTGGATGAAGTGGTGGCGGC  
TGGCAGCACACGGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCTCTGTCTGCCATG  
ACCCCATCAACATCCAGTTACCTCGGGGACAACAGGCAGCCCCAAGGGGGCCACCCTCTCC  
CACTACAACATTGTCAACAACCTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC  
ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCTGTACCATTGCCTGGGTTCCTGGCAG  
GCACAATGATGTGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC  
AAGAAGGCACTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCTGTATGGTACCCCCACGAT  
GTTCTGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG  
GTGTCAATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT  
ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCGTGACATTTCGCGCACTT  
CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGG  
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGGAGCTGTGC  
ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT  
GGATCAGGACAAGTGGTATTGGACAGGAGATGTGCCACAATGAATGAGCAGGGCTTCTGCA  
AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCCGCAGAG  
CTCGAGGACTTCTTTACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA  
CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTTCGGCTGAAGGACGGGGAGGAGACCACGG  
TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCGGAAGTACATC  
GTGTTTGTACAAACTACCCCTCACCATTTAGGAAAGATCCAGAAATTCAAACCTTCGAGA  
GCAGATGGAACGACATCTAAATCTGTGAATAAAGCAGCAGGCCTGTCTGGCCGGTTGGCTT  
GACTCTCTCCTGTCAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCCAGCACCCAGTTC  
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAATAAGAGCTCCTGGATGGGTC  
CGGGAACTCGCTGGGCACAAGGTGCCAAAAGGCAGGCAGCCTGCCAGGCCCTCCCTCCTG  
TCCATCCCCACATTCCCCTGTCTGTCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT  
GAAAAAAAAAAAAAAAAA



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**FIGURE 122**

MAVYVGMLRLGRLCAGSSGVLGARAALSRSWQEARLQGVRFLSSREVD RMVSTFIGGLSYVQ  
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG  
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY  
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLP GTLLLDEVVAAGSTRQHLDQLQYN  
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY  
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY  
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG  
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT  
MNEQGFCIKIVGRSKDMIIRGGENIYPAELEDDFFHTHPKVQEVQVVGVKDDRMGEEICACIRL  
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domains:**

amino acids 140-161, 213-229, 312-334

**Putative AMP-binding Domain Signature:**

amino acids 260-271

**N-myristoylation Sites:**amino acids 19-24, 22-27, 120-125, 203-208, 268-273, 272-277,  
314-319, 318-323, 379-384, 380-385, 409-413**N-glycosylation Site:**

amino acids 282-285

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**FIGURE 123**

CAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA  
TGATCCTGCCCCAACCCCTGTACCATTGCCTGGGTTCCTGGCAGGCACAATGATGTGTCTG  
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGCAAGAAGGCACTGGAGGC  
CATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGATGTTCTGTTGGACATTCTGA  
ACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAGGTGTCATTGCTGGGTCC  
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT  
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTTCCCTGAGGACACTGTGG  
AGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGGCGCGGATCATGAACATG  
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCCGGGGAGCTGTGCATCCGAGGGTACTGCGT  
CATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT  
ATTGGACAGGAGATGTCGCCAC

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**FIGURE 124**

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCCAGGCCATGATCTGGACTGC  
AGGCTGGCTGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG  
TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC  
GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC  
AGTGCGGGGTTGCGGTTTCGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC  
TTCTGGCGTTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC  
ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCAACGGCGTGGAGTG  
CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCCGGTCGTGAGCT  
GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTCACCTTGACGGCA  
GCTAATGTGACTGTGTCTTGCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA  
TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAAC  
CTGACCTCCGCAACAAGACCTACTTCTCCCCCTCGAATCCCACCCCTTGTCGGGCTGCCCCCT  
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAG  
ACCCACATCCACCACCAAAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG  
AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC  
CGCAGCAATTCAGGGCAGTATCCTGCAAAAGGGGGGCCCCAGCAGCCCCATAATAAAGGCTG  
TGTGGCTCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCTTACTGT  
GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT  
CATCACTTCCTGTTCCCACTGACTGGGCTGGCCCAGCCCCTGTTTTTCCAACATTCCC  
CAGTATCCCCAGCTTCTGCTGCGCTGGTTTGCGGCTTTGGGAAATAAAATACCGTTGTATAT  
ATTCTGCCAGGGGTGTTCTAGCTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC  
TCCGCTTGTCTCTTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTCACGGGGAAGGTG  
AGAGAGAGGATGCTAAGCTTCCTACTCACTTTCTCCTAGCCAGCCTGGACTTTGGAGCGTGG  
GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG  
GAATCGGTTCCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC  
CCAATTCGCCCTATAGTGAGTCGTA

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**FIGURE 125**

MDPARKAGAQAAMIWTAGWLLLLLLRGGAQALECYSCVQKADDGCS PNKMKT VKCAPGVDVCT  
EAVGAVETIHGQFSLAVRGCGSLPGKNDRGLDLHGLLAFIQLQQCAQDRCNAKLNLT SRAL  
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCDFGNVTLTAANVTV  
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRI PPLVRLPPPEPTT  
VASTTSVTTST SAPVRPTSTTKPMPAPTSQT PRQGV EHEASRDEEPRLTGGAAGHQDRS NSG  
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

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**FIGURE 126**

CGGGACTCGGCGGGTCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCCATGGAGT  
TGGTGCTGGTCTTCCTCTGCAGCCTGCTGGCCCCCATGGTCCTGGCCAGTGCAGCTGAAAAG  
GAGAAGGAAATGGACCCTTTTCATTATGATTACCAGACCCTGAGGATTGGGGGACTGGTGTT  
CGCTGTGGTCCTCTTCTCGGTTGGGATCCTCCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT  
TCAATCAGAAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACCGCC  
AATGCAACAGAGCCCCAGAAGCAGAGAACTGAAGTGCAGCCATCAGGTGGAAGCCTCTGGAA  
CCTGAGGCGGCTGCTTGAACCTTTGGATGCAAATGTCGATGCTTAAGAAAACCGGCCACTTC  
AGCAACAGCCCTTTCCCCAGGAGAAGCCAAGAACTTGTGTGTCCCCACCCTATCCCCTCTA  
ACACCATTCCCTCCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGGTCTCT  
GCCACCTCCCGTGATGTGTGTGTGTGTGTGTGTGTGTGACTGTGTGTGTTTGCTAACTGTG  
GTCTTTGTGGCTACTTGTTTGTGGATGGTATTGTGTTTGTAGTGAAGTGTGGACTCGCTTT  
CCCAGGCAGGGGCTGAGCCACATGGCCATCTGCTCCTCCCTGCCCCCGTGGCCCTCCATCAC  
CTTCTGCTCCTAGGAGGCTGCTTGTTGCCGAGACCAGCCCCCTCCCCTGATTTAGGGATGC  
GTAGGGTAAGAGCACGGGCAGTGGTCTTCAGTCGTCTTGGGACCTGGGAAGGTTTGCAGCAC  
TTTGTCAATCATCTTCATGGACTCCTTTCACTCCTTTAACAAAAACCTTGCTTCCTTATCCC  
ACCTGATCCCAGTCTGAAGGTCTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGAGCC  
CAGCGTTGACGTCAGGCAGGCTATGCCCTTCCGTGGTTAATTTCTTCCCAGGGGCTTCCACG  
AGGAGTCCCCATCTGCCCCGCCCTTCACAGAGCGCCCCGGGATTCCAGGCCCAGGGCTTCT  
ACTCTGCCCCCTGGGGAATGTGTCCCCTGCATATCTTCTCAGCAATAACTCCATGGGCTCTGG  
GACCCTACCCCTTCCAACCTTCCCTGCTTCTGAGACTTCAATCTACAGCCCAGCTCATCCAG  
ATGCAGACTACAGTCCCTGCAATTGGGTCTCTGGCAGGCAATAGTTGAAGGACTCCTGTTCC  
GTTGGGGCCAGCACACCGGGATGGATGGAGGGAGAGCAGAGGCCTTTGCTTCTCTGCCTACG  
TCCCCTTAGATGGGCAGCAGAGGCAACTCCCGCATCCTTTGCTCTGCCTGTGCGTGGTCAGA  
GCGGTGAGCGAGGTGGGTGGGAGACTCAGCAGGCTCCGTGCAGCCCTTGGGAACAGTGAGAG  
GTTGAAGGTCATAACGAGAGTGGGAACTCAACCAGATCCCGCCCCCTCCTGTCTCTGTGTT  
CCCGCGGAAACCAACCAAACCGTGCGCTGTGACCCATTGCTGTTCTCTGTATCGTGATCTAT  
CCTCAACAACAACAGAAAAAGGAATAAAATATCCTTTGTTTCCT

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**FIGURE 127**

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRCK  
CSFNQKPRAPGDEEAQVENLITANATEPQKQRTQVQPSGGSLWNLRRLLLEPLDANVDA

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**FIGURE 128**

AAACTTGACGCC**ATGA**AAGATCCCGGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT  
CCTCTGCCCAGGGAGCCACCCTGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG  
CGTCACGACCCGAGGCCTTTAACACCCCGTTCCTGAACATCGACAAATTGCGATCTGCGTTT  
AAGGCTGATGAGTTCCTGAACTGGCACGCCCTCTTTGAGTCTATCAAAGGAACTTCCTTT  
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCCAGT  
**G**ACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT  
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTTCCATCCAAA

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**FIGURE 129**

MKIPVLPVVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE  
FLNWHALFESIKRKLPFLNWDAFPKLKGLRSATPDAQ



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**FIGURE 130**

CAGTTCTGAAATCAATGGAGTTAATTTAGGGAATACAAACCAGCC**ATG**GGGGTGGAGATTGC  
CTTTGCCTCAGTGATTCTCACCTGCCTCTCCCTTCTGGCAGCAGGAGTCTCCCAGGTTGTTC  
TTCTCCAGCCAGTTCCAACCTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC  
TTTGCCGGCCACTCA**TGAG**AGTGTTTTTGTGTAAAGTATTTTTTAGAATACTGTTGACTTCT  
TCATGATTTAATAACCATCCTTTGCGAAGTTTTATGAGGCTTTAGGGGAATGTCAACCCTCA  
AATTTTTGTTATACTAGATGGCTTCCATTTACCCACCACTATTTTAAGGTCCCTTTATTTTT  
AGGTTCAAGGTTCAATTTGACTTGAGAAAGTGCCCTTCTGCAGCTTCATTGATTTTGTATC  
TTCATATTAATTGTAACGATTAAAAAGAATAAGAGCACGCAGACCTCTAGGAGAATATTT  
TATCCCTGGGTGCCCCTGACACATTTATGTAGTGATCCCACAAATGTGATTGTTAATTTAA  
TGTTATTCTAATATTAGTACATTCAGTTGTGATGTAATATGAATAACCAGAATCTATTTCTT  
AAAAGTTTTGAGTATATTTTTCAACTAGATATTTGTATAGAAAGACTGAATAGTGATG

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**FIGURE 131**

MGVEIAFASVILTCLSLAAGVSQVLLQPVPTQETGPKAMGDLSCGFAGHS

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**FIGURE 132**

GGGGAATCTGCAGTAGGTCTGCCGGCG**ATG**GAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG  
GCTGCTGTTGTTCCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAATGGA  
AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC  
TGCAGCTGCTACCATGGTGT CATAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG  
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA  
GACTGTACCGGGAAAATGACTGCATGTTCCCTCAAGGTGTAGTGGTGTGAGCACTTTATT  
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA  
GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC  
ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT  
CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTGAGCAGCACAGTG  
GCCATGGAAAAAGAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG  
ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACCTGTTGATGCAGAATACACCAAAAAC  
CAGGCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT  
GGATCACTGCAAATACAAGTATCTGTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA  
AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC  
TATCCACAGCTGAAGCCATGGGTTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA  
AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA  
GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG  
AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT  
TCCCAAATGTTGAAAACCTGAAGTAT**TAG**TAGTCATCATAGGACCATAGTCCTCTTTGTGGCA  
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA  
TCTGCTATCAAGCCAAATACCTGGTTTTCTTATCATGCTGCACCCAGAGCAACTCTTGAGA  
AAGATTTAAATGTGTCTAATACTGATATGAAGCAGTTCAACTTTTTGGATGAATAAGGA  
CCAGAAATCGTGAGATGTGGATTTTGAACCAACTCTACCTTTCATTTTCTTAAGACCAATC  
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA  
TGTGATGATGCCCTTTGTCCCATTTTGGAGCAGAAAATTCGTCATTTGGAAGTAGTACAA  
CTCATTGCTGGAATTGTGAAATTATTCAAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG  
AAACCCTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG  
TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAACCATAAACTCTGTTACTCAG  
GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT  
TCAGGTTCCCTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

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**FIGURE 133**

MEWWASSPLRLWLLLFLLPSAQGRQKESGSKWKVFIDQINRSLENYEPCSSQNCSCYHGVIE  
EDLTPFRGGISRKMMAEVVRRKLGTHYQITKNRLYREND CMFPSRCSGVEHFILEVIGRLPD  
MEMVINVRDYPQVPKWMEDIAIPVFSFSKTSEYHDIMYPAWTFWEGGPAVWPYPTGLGRWDL  
FREDLVRSAQWPWKKNSTAYFRGSRTSPERDPLILLSRKNPKLVDAEYTKNQAWKSMKDT  
LGKPAAKDVHLVDHCKYKYLNFNFRGVAASFRFKHLFLCGSLVFHVGDEWLEFFYPQLKPWVH  
YIPVKTDLSNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMDDITCYWENLLSEYSKFLSY  
NVTRRKGYDQIIPKMLKTEL

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**FIGURE 134**

CACCCCTCCATTTCTCGCC**ATG**CCCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT  
TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTTACCTCCCTTCGGCCACTTCTT  
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCCCGCCAGGGATGGCTGGCTGCCCTGCAGGA  
CCGCAGCATCCTTGCCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC  
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCCCTTCAG  
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGCACTGGTGATGCGGTACTGGGAGCC  
CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC  
TCCTCTGCTTTGTGCTCCATGTCATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT  
GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC  
TCTGGCCCTGAAGTCTCCCCGGGCTCTCAGACTCTTCTCCACCTGCGCCACCCAGTGTGTG  
TGGAGCTGCTGACAGTGCTGTGGGTGGTGCCTACCTGGGCACGGACCGTCTCCTCCTTGCT  
TTCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT  
CCGGGCCCAGCTACAAAGAAAACCTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT  
**G**AGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCTCTCCCACTGAATTCTAAATCCTTAAC  
ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCTT  
CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA  
CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC  
TTCCTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC  
CTGACCACTCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCTTCTGCACCGCT  
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA  
GGCCCCAACCTTGCCTCACCCTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT  
GGGCTCAGACCCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACCTCGATGACTTGGGGCTC  
CCTGCTCTCCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTTTCTAAAAAAA

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## **FIGURE 135**

MAPALLLI PAALASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAAALQDRSILAP  
LAWDLGLLLLFVGQHSLMAAERVKAWSRYFGVLQRSLYVACTALALQLVMRYWEPIPKGPV  
LWEARAEPWATWVPLLCFVLHVISWLLIFSILLVFDYAELMGLKQVYYHVLGLGEPLALKSP  
RALRLFSLRHPVCVELLTVLWVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR  
KLHLLSRPQDGEAE

**Signal sequence:**

amino acids 1-13

**Transmembrane domains:**

amino acids 58-76, 99-113, 141-159, 203-222

**N-myristoylation sites:**

amino acids 37-43, 42-48, 229-235

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**FIGURE 136**

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA  
AGAAATTGCCAAACCATGTCTTTTTTCTGTTTTTCAGAGTAGTTCACAACAGATCTGAGTGT  
TTTAATTAAGCATGGAATACAGAAAACAACAAAAAAGCTTAAGCTTTAATTTTCATCTGGAATT  
CCACAGTTTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTTCCCGCTGGCTGCTCTA  
TCACGTGGTGCTCTCCGACTACTCACCCCGAGTGTAAGAACCTTCGGCTCGCGTGCTTCTG  
AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCTTCCGAGTAGGATGTCACTGAGATCC  
CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT  
TCCCCACTACAATGTGATAGAACGCGTGAAGTGGATGTACTTCTATGAGTATGAGCCGATTT  
ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAAAGTCTCTCATCAAAATCCATTT  
CTGGTCATTCTGGTGACCTCCCACCCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC  
TTGGGGTGAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG  
AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTTATGGT  
GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTTATGGC  
ATTGAGGTGGGTAACTGAGTTTTGCCCAATGCCAAGTACGTAATGAAGACAGACACTGATG  
TTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT  
TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT  
TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTTGGGTATATAA  
TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGTCACGTAAAACCCATCAAGTTT  
GAAGATGTTTATGTCGGGATCTGTTTGAATTTATTAAGTGAACATTCATATTCCAGAAGA  
CACAAATCTTTTCTTTCTATATAGAATCCATTTGGATGTCTGTCAACTGAGACGTGTGATTG  
CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTTTTGGCAGGTCATGCTAAGGAACACC  
ACATGCCATTATTAAGCTTCACATTCTACAAAAAGCCTAGAAGGACAGGATACCTTGTGGAAA  
GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG  
AACTGAAACTCATGAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC  
AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGTCTAAA  
GAAATTAATAGGACCAACAATTTGGACATGTCATTCTGTAGACTAGAATTTCTTAAAAGGG  
TGTTACTGAGTTATAAGCTCACTAGGCTGTAAAAACAAAACAATGTAGAGTTTTATTATTG  
AACAATGTAGTCACTTGAAGGTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA  
TGTAAGTCTGTGTCAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT  
TGGTCATTTATAAAGTACTTCAAGATGTTGCAGTATTTACAGTTATTATTATTTAAATTA  
CTTCAACTTTGTGTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAGGATAGTGAAT  
CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC  
TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTAAAT  
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAA

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**FIGURE 137**

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPiYRQD  
FHFTLREHSNCSHQNPFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFLLGQEA EK  
EDKMLALSLEDEHLLYGDIIRQDFLDTYNNLTLKTIMAFRWVTEFCPNAKYVMKTD TDVFIN  
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD  
LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG  
FSSKEIITFWQVMLRNTTCHY



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**FIGURE 138**

CCTCTGTCCACTGCTTTCGTGAAGACAAGATGAAGTTCACAATTGTCTTTGCTGGACTTCTT  
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA  
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA  
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC  
AGACTCTTTCAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT  
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC  
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA  
AAAAACATTGCAAACATGTGTCGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC  
AAGCCTGTTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT  
CCTTCTGTGGAGACACGGTGGAGAACTAAACAATTTTTTAAAGCCACTATGGATTTAGTCAT  
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTACCATGTCATTCTGAAATT  
TTTCTCTACTAGTTATGTTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAA

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**FIGURE 139**

MKFTIVFAGLLGVFLAPALANYNINVNDNNNAGSGQQSVSVNNEHNVANVDNNNGWDSWNS  
IWDYGNNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPKGLMYSVN  
PNKVDDLKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

**Signal Peptide:**

amino acids 1-20

**N-myristoylation Sites:**

amino acids 67-72, 118-123, 163-168

**Flavodoxin protein homology:**

amino acids 156-174

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**FIGURE 140**

CATTTCTGAACTAATCGTGTCAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA  
TTAACTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG  
CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTCTTATTGCTTACTGATTTTTT  
TGAGTTAAGAGTTGTTATATGCTAGAAATATGAGGATGTGAATATAAATAAGAGAAGAAAAA  
GAATAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTTTACATG  
CAAGCTTATAGTTGAAATATTTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGT  
TTGTTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT  
CAGATTCCGTTGCCAACTCGTCCCCATTGGTTTCTTCTTTTTGGTACTACAGAAGAGGAAAT  
CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAGCCAACTATGAATTAC  
TGGAAAAAGAAGTAGAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTAAAAGCAAAGGGA  
TTGAATCCGGATGGAACCTCCAGCCCTTCAACCCTGGGTGGATTTTCTCCAGCTCCAAGCC  
ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG  
TCAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCTTACAATGGTGTAAGAAAA  
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAAGTCGATCGAGGTCAAGAACACGATCACG  
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA  
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT  
GGTTCTCCTCACCTTAAGGCCAAGCATAACCAGAGATGATTTAAAAGTTCAAACAGACATGG  
TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG  
CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT  
GAGAGGTCCCATAAAAGCAAGCACCATGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG  
CTGACTTTCTCTTCTTTGAGCCTGCATCAGTTCTTGGTTTTGCCTATCTACAGTGTGATGT  
ATGGACTCAATCAAAAACATTAAACGCAAACCTGATTAGGATTTGATTTCTTGAAACCTCTA  
GGTCTCTAGAACACTGAGGACAGTTTCTTTTGAAAAGAACTATGTTAATTTTTTGCACATT  
AAAATGCCCTAGCAGTATCTAATTA AAAACCATGGTCAGGTCAATTGTACTTTATTATAGT  
TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT  
ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT  
ACTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTACAAGGAAATAAAATACAAAT  
CTTGTTTTTTCTAAAAA AAAAAAAAAAAGT

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**FIGURE 141**

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLLFGTTEEEIQEICIETLRLY  
TRKKPNYELLEKEVEKRRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEK  
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN  
NRRSRSGTYSSRSRSHSESPPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRKKSRSRSQ  
SKSRDHSDAAKKHRHERGHRDRRERSRSFERSHKSKHHGGSRSRSGHGRHRR

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**FIGURE 142**

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTTATCA  
TTTTTTGAANNTATTTCGGGTCANAATTGNCTTTGAAAAGCATTGCTTTTTACAGAAATATAT  
TANCTTTTTAGAGTAATTTCTAGTTTGGATTGTAATATGAAATTATTTAAAAGGGCTTCGCT  
CATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTNNTATTGCTTACTGATTTTTTTTG  
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAAGA  
ATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTTTACATGCA  
AGCTTATAGTTGAAATATTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGTTT  
GTTCGATTTCAACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAGNTAGAGCACTTCA  
GATTCCGTTGCCAACTNGTCCCCATTGGTTTCTTCTTTTGGTACTACAGAAGAGGAAATCC  
AGGAAATNTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAACTATGAATTACTG  
GAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCNAATTAAAAGCAAAGGGATT  
GAATCCGGATGGAAGCTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCC

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**FIGURE 143**

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGCACCGCGTTCTCGCACGCGTCATGGC  
GGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC  
CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAAACGGCAGTTTGTTCGATACAAGCACCCG  
TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG  
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG  
AGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCTGCGCTTCTTCCTGGAGTACCAGTGG  
TTTGTGGAÇTTTGGTGTGTACTCGGGCGGCGTGACCTCTTCACAGAGGCCTACTACTACAT  
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCTGCTCACGGTGACCTTCT  
CCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGTGAGCGC  
TCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG  
GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC  
CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG  
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC  
CCAGACCCACCGGGACGCACTGACCATGTGCGAGGACAGACCCATGCTGCAGTTCTCTCCTGC  
ACACCAGCTTCCTGTCTCCCCTGTTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC  
TTCTTGCAACCAGCCGCCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA  
CTCTGGGCGCCTCTGGTTGCTGGTGGTGTGCTGTGCCTGCTGCGGCTGGCGGTGACCCGGCCCC  
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC  
CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT  
GAGCTTGCAGTACCTGACGCGCTCATCCTCACCCCTCAACTGCACACTTCTGCTCAAGACGC  
TGGGAGGCTATTCTTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCGACCCATCCTCAGCC  
AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG  
GGCCCTGGGTGGCCTGCTTACTCCCCCTTTCCTCCGTGGCGTCCCTGGCCTACCTCATCTGGT  
GGACGGCTGCCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA  
GGCTCCTAGCTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCTGGGGCAGCGGGACA  
CTAGCCTGCCCCCTCTGTTTGCGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC  
GGCGTTCCCTTCACCACAGTGCCTGACCCGCGGCCCCCCTTGGACGCCGAGTTTCTGCCTCA  
GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG  
TGCCAGGTTTGAGTGCGGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC  
GATTTTAA

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**FIGURE 144**

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE  
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY  
YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGGERSVCLTFAFLFLLAMLVQV  
VREETLELGLEPGLASMTQNLEPLLKKQGDWALPVAKLAIRVGLAVVGSVLGAFLTFFGLR  
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA  
FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT  
VVSLOYLTPILTLNCTLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAAARI  
AGALGGLLTPLFLRGVLAYLIWWTAAACQLLASLFGLYFHQHLA

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**FIGURE 145**

CGTTNGCACGCGTCAATGGCGGTCCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCAC  
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTT  
TGTTCCGATACAAGCACCCGTNTTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCC  
CAGAGGCAGGAAAGAGCGGTGGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCC  
GAGATGCCCCGTTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCTGCGC  
TTCTTCCTGGAGTACCAGTGGTTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGACCTCTT  
CACAGAGGCCTACTACTACATGCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT  
GCCTGCTCACAGTGACCTTCTCCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGC  
GCCGAGGAGGGGGGTGAGCGCTCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGC  
CATGCTGGTGCAAGCG



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**FIGURE 146**

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGCCCCGTGATTTATTAACTGGGCTT  
AATCTGAAGGTTCTCAGTCAAATTTCTTGTGATCTACTGATTGTGGGGGCATGGCAAGGTTTGTCTAAAGGAGC  
TTGGCTGGTTTGGGCCCTTGTAGCTGACAGAAGGTGGCCAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGG  
CGCTTCTGTTGCTGGTCTTGCCTTGGCTCAGTCCTGCTAACTACATTGACAATGTGGGCAACCTGCACTTCCTG  
TATTCAAGACTCTGTAAAGGTGCCTCCCACTACGGCCTGACCAAGATAGGAAGAGGCGCTCACAAGATGGCTG  
TCCAGACGGCTGTGCGAGCCTCACAGCCAGGGCTCCCTCCCCAGAGGTTTCTGCAGCTGCCACCATCTCCTTAA  
TGACAGACGAGCCTGGCCTAGACAACCTGCCTACGTGTCTCGGCAGAGGACGGGCAGCCAGCAATCAGCCCA  
GTGGACTCTGGCCGGAGCAACCGAAGTAGGGGCACGGCCCTTTGAGAGATCCACTATTAGAAGCAGATCATTTAA  
AAAAATAAATCGAGCTTTGAGTGTTCTTGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGG  
GCAGGGAATTTCTGAAAACACCCTGCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAA  
ATTACCAGCATCAAGATCAATCGAGTAGATCCCAAGTGAAGCCTCTCTATTAGGCTGGTGGGAGGTAGCGAAAC  
CCCCTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAGAGACGGCCGGCTACTGCCAG  
GAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATGTCCCTCACAACCTACGCTGTGCGTCTCTGCGG  
CAGCCCTGCCAGGTGCTGTGGCTGACTGTGATGCGTGAACAGAAAGTCCGCAGCAGGAACAATGGACAGGCCCC  
GGATGCCCTACAGACCCCCGAGATGACAGCTTTTATGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGAA  
TAAACTGGTGCGCAAGGTGGATGAGCCTGGGGTTTTTATCTTCAATGTGCTGGATGGCGGTGTGGCATATCGA  
CATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCGATATGGCAGCCCAGAAAG  
TGCGGCTCATCTGATTACAGGCCAGTGAAAGACGTGTTACCTCGTGTGCTCCCGCCAGGTTTGGCAGCGGAGCC  
CTGACATCTTTCAGGAAGCCGGCTGGAACAGCAATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGGAGCAACACT  
CCCAAGCCCTCCATCCTACAATTACTTGTGATGAGAAGGTGGTAAATATCCAAAAAGACCCCGGTGAATCTCT  
CGGCATGACCGTCGCAGGGGAGCATCACATAGAGAAATGGGATTTGCCTATCTATGTCATCAGTGTGAGCCCCG  
GAGGAGTCATAAGCAGAGATGGAAGAATAAAAACAGGTGACATTTTGTGTAATGTGGATGGGGTCGAACTGACA  
GAGGTGAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCATCCTCGATAGTACTCAAAGCTTTGGAAGT  
CAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGCCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCA  
GTGACTGGTCCCCATCCTGGGTCATGTGGCTGGAATTACCACGGTGCTTGTATAACTGTAAAGATATTGTATTA  
CGAAGAAACACAGCTGGAAGTCTGGGCTTCTGCATTGTAGGAGGTTATGAAGAATACAATGGAACAAACCTTT  
TTTCATCAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGGTGATATTCTTCTTG  
CTGTCAATGGTAGAAGTACATCAGGAATGATACATGCTTGCTTGGCAAGACTGCTGAAAGAATTAAAGGAAGA  
ATTACTCTAACTATTGTTTCTTGGCCTGGCACTTTTTTATAGAATCAATGATGGGTGAGGAAAAACAGAAAAA  
TCACAAATAGGCTAAGAAGTTGAACACTATATTTATCTTGTGAGTTTTTATATTTAAAGAAAGAAATACATTGT  
AAAAATGTCAGGAAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAATATGATTCCAAAAAATTA  
AACTACTAGTTTTTTTTTCAAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTTTTTCTATTCAAT  
AAAAAGCCCTAAAACAATAAATGATTGATTTGTATACCCCACTGAATTCAAGCTGATTTAAATTTAAATTT  
GGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCATTTTAAATTTACAGCTAAAATATTTTTTAAATGCA  
TTGCTGAGAAACGTTGCTTTTCATCAAACAAGAATAAATATTTTTTCAAGATTAA

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**FIGURE 147**

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPCDGCASLTAT  
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS  
FKKINRALSVLRRTKSGSAVANHADQGRESENTTAPFVFPRLYHLIPDGEITSIKINRVDP  
SESLSIRLVGGSETPLVHIIIQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL  
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQLGIKLVKVDPEGV  
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESAHLIQASERRVHLVSRQVRQRS  
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNQKDPGESLGMTVAGGASHRE  
WDLPIYVISVEPGGVISRDGRIKTGDILLNVVGVELTEVSRSEAVALLKRTSSSIVLKALEV  
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV  
GGYEEYNGNKPFFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI  
TLTIVSWPGTFL

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**FIGURE 148**

CCAAAGTGATCATTTGAAAAAGAGATATCCACATCTTCAAGCCCATATAAAGGATAGAAGCT  
GCACAGGGCAGCTTTACTTACTCCAGCACCTTCCTCTCCCAGGCAAATGGTGCTGACCATCT  
TTGGGATACAATCTCATGGATACGAGGTTTTTAACATCATCAGCCCAAGCAACAATGGTGGC  
AATGTTTCAGGAGACAGTGACAATTGATAATGAAAAAATACCGCCATCGTTAACATCCATGC  
AGGATCATGCTCTTCTACCACAATTTTTGACTATAAACATGGCTACATTGCATCCAGGGTGC  
TCTCCCGAAGAGCCTGCTTTATCCTGAAGATGGACCATCAGAACATCCCTCCTCTGAACAAT  
CTCCAATGGTACATCTATGAGAAACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG  
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCCTGCTTGGGTCAC  
CCATTGAGAAACTCTGCAAACATATCCCTTTGTATAAGGGGGAAGTGGTTGAAAACACACAT  
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGGCTCCTGGGCATCTTGGGAATTTCAATCTG  
TGCAGACATTCATGTTTAGGATGATTAGCCCTCTTGTTTTATCTTTTCAAAGAAATACATCC  
TTGGTTTACTACTCAAAGTCAAATTAAATTCTTTCCCAATGCCCCAACTAATTTTGAGATTC  
AGTCAGAAAATATAAATGCTGTATTTATA

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**FIGURE 149**

MKILVAFLVLTIFGIQSHGYEVFNIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT  
IFDYKHGYIASRVLSRRACFILKMDHQNIPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE  
SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

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**FIGURE 150**

GGCACGAGCCAGGAACTAGGAGGTTCTCACTGCCCGAGCAGAGGCCCTACACCCACCGAGGC  
**ATG**GGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG  
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCCTGGAAGTTTTCCCAAAG  
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCCAGCCACCACCGCCCATCACCTATTCCCTC  
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT  
CAACCTCAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT  
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG  
CCAGTGTCTGAGCTGCGGGCCAACCTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA  
GATGATCTGCCAGGCGTCCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAGGATG  
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCTGCCG  
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC  
CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA  
GCCCCATCCTTGCCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG  
GGGTTCAGGATAGGGAATGGGGAGGTCAGAGGACGCAAAGCAGCAGCCATG**TAG**AATGAACC  
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTCGTATTTGGA  
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 151**

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL  
CGTKNIKVAKKVVKTHEPASFNLNVTLKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK  
PVSELNANFTLQDRGAGPRVEMICQASSGSPITNSLIGKDGQVHLQQRPCHRQPANFSFLP  
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG  
GFRIGNGEVRGRKAAAM

**Signal Peptide:**

amino acids 1-18

**N-glycosylation Sites:**

amino acids 86-89, 132-135, 181-184

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**FIGURE 152**

GGTCCTTA**ATG**GCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG  
CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCTCACTCTCTTTGCTATGACATCACCGT  
CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA  
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGGAAGAAA  
CTAAATGTCACAACGGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT  
TACAGAGCAACTGCGTGACATTGAGCTGGAGAATTACACACCCAAGGAACCCCTCACCCCTGC  
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT  
TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC  
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT  
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC  
CTGGAGCCAAGTGCAGGAGCACCCTCGCCATGTCCTCAGGCACAACCCAACTCAGGGCCAC  
AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA  
TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAGGCTCCTGTGAGCACG  
GTCTTGATCAAACCTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT  
GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCCTT  
TTGCCAACAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTTGGTGCTACC  
TGATGGAATTCCTGCACTTAAAGTTCTGGCTGACTAAACAAGATATATCATTTTCTTTCTTC  
TCTTTTTGTTTTGGAAAATCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATT  
GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG  
AATTTTAAATTTAATAAGAAAAAATTTATATTAATGATTGTTTCCTTTAGTAATTTAT  
TGTTCTGTACTGATATTTAATAAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 153**

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL  
HYDCGNKTVTPVSPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR  
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS  
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

**Important features:****Signal peptide:**

amino acids 1-25

**Transmembrane domain:**

amino acids 224-246

**N-glycosylation site.**

amino acids 68-72, 82-86

**N-myristoylation site.**

amino acids 200-206, 210-216

**Amidation site.**

amino acids 77-81



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**FIGURE 154**

GGGAAAGCCATTTTCGAAAACCCATCTATACAACTATATATTTTCATTTCTGCTGCTAGCTG  
CCTTGGGCCTCACAATTTTCATTCTGTTTTCTGACTTTCAAGTTATATACCGTGGAATGGAG  
TTGATCCCAACCATAACATCGTGGAGGGTTTTAATTTTGGTGGTAGCCCTCACCCAATTCTG  
GTGTGGCTTTCTTTGCAGAGGATTCCACCTTCAAAATCATGAACTCTGGCTGTTGATCAAAA  
GAGAATTTGGATTCTACTCTAAAAGTCAATATAGGACTTGGCAAAAGAAGCTAGCAGAAGAC  
TCAACCTGGCCTCCCATAAACAGGACAGATTATTCAGGTGATGGCAAAAATGGATTCTACAT  
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAATCAAATTGGGAGGCCAAC  
CCACAGAACAGCATTTCTGGGCCAGGCTGTAATCAGAATTGTCGTCGTACATGCTCAACAGC  
ATTGCTTTTTTCCCCAAAATTAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTTT  
CCTCTCTCCATTCAAGCATTCAAAGTATATTTTCAATGAATTAAACCTTGCAGCAAGGGACC  
TTAGATAGGCTTATTCTGACTGTATGCTTTACCAATGAGAGAAAAAAATGCATTTCTGTAT  
CATCCTTTTCAATAAACTGTATTCATTTGAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 155**

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHFWLLIKREFGFYSKSQYRTWQKKLA  
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL

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**FIGURE 156**

GTTCTCCTTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACC**ATGAAG**  
CTCTTGTGGCAGGTAAGTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTTCGTCTA  
CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC  
AGAACTGCCCTCCGTTTGCTCGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCACGCGCCGG  
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA  
CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCCTGCAGT  
TGGGCAGGAAGTCCATCCGGCAGATTGAGGTGGGGGCCTTCAACGGCCTGGCCAGCCTCAAC  
ACCCTGGAGCTGTTTCGACAACTGGCTGACAGTCATCCCTAGCGGGGCCTTTGAATACCTGTC  
CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA  
ACCGGGTGCCCTCCCTCATGCGCCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT  
GAGGGAGCTTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACTGGGCATGTGCAACATTAA  
AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTGAGGGAACCACT  
TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTGATG  
AACTCACAGGTCAGCCTGATTGAGCGGAATGCTTTTGACGGGCTGGCTTCACTTGTGGAAGT  
CAACTTGGCCCACAATAACCTCTCTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC  
TGGTGGAGTTGCATCTACACCACAACCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC  
TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTCATGCTCCCAT  
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT  
TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTTCGGATGGCAGAACTTAAGTGT  
CGGACTCCCCCTATGTCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC  
CTCCCGCCACCCAAGGATCTCTGTCTCAACGACGGCACCTTGAACTTTTCCACGTGCTGC  
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG  
GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTACCACAGT  
AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTTA  
CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTCAGACTACC  
CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT  
GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG  
CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC  
ACAGCCGCCCCGACTGTTGAGATAATCCAGGTGGACGAAGACATCCCAGCAGCAACATCCGC  
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCACAATTC  
ATGACCATATTAACATAACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAACAGC  
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTCTGAACCTTATATAATTCAGACCCA  
TACCAAGGACAAGGTACAGGAACTCAAATAT**TGACT**CCCCTCCCCCAAAAACTTATAAAAT  
GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTTCTTGTA  
TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAATAATTTAAAGA  
CAAAAAGTCAAAACA

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**FIGURE 157**

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVCT  
RRGLSEVPQGIPSNTRYLNLMENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS  
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY  
ISEGAFEGLFNLKYLNLGMCNIKDMPNLTPLVGLEEELEMSGNHFPPEIRPGSFHGLSSLKKLW  
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLP HDLFTPLRYLVELHLHNPWNCD CDILW  
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL  
KCRTPPMSSSVKWL LPNGTVLSHASRHPRISVLNDGT LNFSHVLLSDTGVYTCMVTNVAGNSN  
ASAYLNVSTAE LNTSNYSFFT VTVETTEISPEDTTRKYKVPVTTSTGYQPAYTTSTTVLIQ  
TTRVPKQVAVPATD TTDKMQTS LDEVMKTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS  
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE  
NSLGNSLHPTVTTISEPYIIQTHTKDKVQETQI

**FIGURE 158**

[illegible]

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**FIGURE 159**

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREVV  
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGLDDEFYVKGFYCAECRAGWYGGD  
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD  
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFSHDGSKNFDGFMHAIYEEITACSSSPCFHDG  
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV  
VSFFCNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPMPVQSRETPLH  
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK  
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE  
RTVVVAAHCVTDLGKVMTIKTADLKVVVLGKFYRDDDRDEKTIQSLQISAILHPNYDPILLD  
ADIAILKLLDKARISTRVQPICLAASRDLSTSFAQESHITVAGWNVLADVRSPGFKNDTLRSG  
VVSVDSSLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR  
WHLMGLVSWSYDKTCSHRLSTAFTKVLFPKDWIERNMK

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**FIGURE 160**

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA  
AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTCACGTAATAAAAAACATGGGC  
TTCAACCTGACTTTCCACCTTTCCTACAAATTCGGATTACTGTTGCTGTTGACTTTGTGCCT  
GACAGTGGTTGGGTGGGCCACCAGTAACTACTTCGTGGGTGCCATTCAAGAGATTCCCTAAAG  
CAAAGGAGTTTATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAGGGAAAACTCTGACT  
AATGAAGCATCCACGAAGAAGGTAGAAGTTGACAACTGTCCTTCTGTGTCTCCTTACCTCAG  
AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC  
CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATC  
CTCGTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTT  
CCTGCAGAGGCAGCAGCTGGATTATGGCATCTACGTCATCCACCAGGCTGAAGGTAAAAAGT  
TTAATCGAGCCAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGAC  
TGCTTTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGA  
GGAGCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTG  
GATATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCT  
AACAACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAG  
AATGAAAATTTCCCGGCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAG  
ACAAAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTACGAGTCTGG  
AGAACAGATGGGTTGAGTAGTTGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATA  
TATCAACATCACAGTGGATTTCTGGTTTGGTGCATGACCCCTGGATCTTTTGGTGATGTTTGG  
AAGAACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTA  
AGAACCTGTTACAGCTCATTGTTGAGCTGAATTTTCCCTTTTGTATTTTCTTAGCAGAGCT  
CCTGGTGATGTAGAGTATAAAACAGTTGTAACAAGACAGCTTCTTAGTCATTTTGATCATG  
AGGGTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGAT  
AAAATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTTGAAGTAATATAT  
TATGGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCT  
CGTCCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTCAATTTATCCTGTACAATCATCT  
GTGAAGTGGTGGTGTGAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCA  
GGACACAGTGAAGTTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGCGCTGCAAAGGCAG  
CAGTAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCAGGTATGCCT  
TCCAGTGATGCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGA  
TTTTGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAATAATAATAATA  
TGCTCTATCAAATACCTCTGTAGTAAAATGTGAAAAAGCAAAA

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**FIGURE 161**

MGFNLT FHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTILILGKGKT  
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV  
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKGKFNRAKLLNVGYLEALKEEN  
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSYFGGVLTALSREQFFKVNG  
FSNNYWGWWGGEDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR  
VWRTDGLSSCSYKLVSV EHNPLYINITVDFWFGA

**Important features:****Signal peptide:**

amino acids 1-27

**N-glycosylation sites:**

amino acids 4-7, 220-223 and 335-338

**Xylose isomerase proteins:**

amino acids 191-201



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**FIGURE 162**

CGTGGGCCGGGGTCGCGCAGCGGGCTGTGGGCGCGCCCGGAGGAGCGACCGCCGCAGTTCTC  
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGCCCCGCA**ATG**  
GCCCAGGCAGTGTGGTCGCGCCTCGGCCGCATCCTCTGGCTTGCCTGCCTCCTGCCCTGGGC  
CCCGGCAGGGGTGGCCGAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA  
CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG  
CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA  
GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTGGGCCACGTGCCCCGGGAATTCCCGG  
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG  
GTCCTCCCCATCACAGAGTTCCTCGTGGGGGACCTTGTTGTACCCAGAACA**ACTTCCCTACC**  
CTGGCCCAGCTCCTATCTCACTAAGACCGTCTTGAAAGTCTCCTTCCTCCTCCAGACCCGA  
GCAACTTCTCAAGACCGCCTTGTTTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG  
GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT  
CAAAGTGGTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA  
CCGGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAAACCCTTCGAGGCATCCAAGTGTTGGGG  
CCCACCCTAATTCCAGACCTTCCAAAAGATGACCGTGACCTTGAACCTCCTGGGGAGCCCTCC  
TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCCTCCCGCTGGAGGAAGGGGAGTGCCACC  
CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCCCTGGGGACTAC  
TGCTTCAGCATCCGGGCCGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT  
GTGGCCCTCCAGAATCCAGCCGGCTGTCTTTGCTTTCCCATGTGCTACACTTATCACTGTGA  
TGTTGGCCTTCATCATGTACATGACCCTGCGGAATGCCACTCAGCAAAAGGACATGGTGGAG  
AACCCGGAGCCACCCTCTGGGGTCAGGTGCTGCTGCCAGATGTGCTGTGGGCCTTTCTTGCT  
GGAGACTCCATCTGAGTACCTGGAATTTGTTGCTGAGAACCACGGGCTGCTCCCGCCCCCTCT  
ATAAGTCTGTCAAACTTACACCGTGT**TGAG**CACTCCCCCTCCCCACCCCATCTCAGTGTTAA  
CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTTATT  
TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC  
CCTCCCTCTCTGTACCCCTGACCCAGCCATTACCCATCTGTACAGTCCAGCCACTGACA  
TAAGCCCCACTCGGTTACCACCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT  
TTGATGCTTGGGGTGTTCGCTGTTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCATTCTCT  
CTCATATTGGCAGATCTGCTGTCCATTGGGGGTTCTCAGTTTCTCCTCCCCAGACAGCCCTAC  
CTGTGCCAGAGAGCTAGAAAGAAGGTCATAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC  
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACACA  
CACACACACACAGAAATATAAACACATGCGTCACATGGGCATTTTCAGATGATCAGCTCTGTA  
TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA  
AGCAGCCCTGACAGGTTCTGGGCCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC  
GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCTGGATGGGGGGCAGGACT  
AATACTGAGTGATTGCAGAGTGCTTTATAAATATCACCTTATTTTATCGAAACCCATCTGTG  
AACTTTTCACTGAGGAAAAGGCCTTGACAGCGGTAGAAGAGGTTGAGTCAAGGCCGGGCGCGG  
TGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA  
GATCGAGACCACCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAATACAAAAAGTT  
AGCCGGGCGTGGTGGTGGGTGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG  
GTGCGAACCCGGGAGGCGGAGCTTGAGTGAGCCAGATGGCGCCACTGCACTCCAGCCTGA  
GTGACAGAGCGAGACTCTGTCTCCA

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**FIGURE 163**

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA  
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHVPGEFPVSVWVTAADCWMCQPVARGF  
VVLPITEFLVGD LVVTQNTSLPWPS SYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ  
MVTEDSVVYYNYSIIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL  
GPTLIQTFQKMTVTNLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLHTFRDPGD  
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVF AFPCATLITVMLAFIMYMTLRNATQQKDMV  
ENPEPPSGVRCCCMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

**Important features of the protein:****Signal peptide:**

amino acids 1-24

**Transmembrane domain:**

amino acids 339-362

**N-glycosylation sites.**

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367



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**FIGURE 165**

MALSSQIWAACLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTH  
FPICIFCCGCCHRSKCGMCCKT

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**FIGURE 166**

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC  
CTGGATCTTCCACCATGTTTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC  
ATCTCCCTGACTGTCTCTTACCCTCCTTCTCGTTTTCATCATAGTGCCAGCCATTTTTTG  
AGTCTCCTTTGGTATCCGCAAACCTCTACATGAAAAGTCTGTTAAAAATCTTTGCGTGGGCTA  
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC  
GGAATCATTGCAAAGGATCCCACTTCACTAGAAGAAGAGATCAAAGAGATTTCGTGGAAGTGG  
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGCC  
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAAGTGG  
GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTCGGCTCAC  
GGTCCTGTGGGGGTTAGGAGTGCTGATTTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC  
TGGCTTTTACAGGGATTAGCCTTCTGGTGGTGGGCACAACCTGTGGTGGGATACTTGCCAAAT  
GGGAGGTTTAAAGGAATTCATGAGTAAACATGTTCACTTAATGTGTTACCGGATCTGCGTGCG  
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT  
GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGCCAGCGATGGCTATTATGCC  
ATGGTGGGTCAAGTGCACGGGGGACTCATGGGTGTGATTCAGAGAGCCATGGTGAAGGCCTG  
CCCACACGTCTGGTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA  
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC  
AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC  
TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA  
TGGTGACGTACCTGCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG  
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTGCGAATAGGGTGAAATCTGC  
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGGATGGGGCCCTGAAGAGGGAGAAGG  
TGAAGGACACGTTCAAGGAGGAGCAGAGAAGCTGTACAGCAAGATGATCGTGGGGAACCAC  
AAGGACAGGAGCCGCTCCTTGAGCCTGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA  
CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCCTGCTGTGTCTTTCCAGACTCCAGGG  
CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT  
GCACCCGGCGCAGCCTACCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA  
CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACTCCCCA  
CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT  
GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGCGGCCACCCG  
CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC  
CTTGAGCTCTGCAGACATGATAGGAAGGAACTGTATCTGCAGGGGCTTTCAGCAAAATG  
AAGGGTTAGATTTTTATGCTGCTGCTGATGGGGTTACTAAAGGGAGGGGAAGAGGCCAGGTG  
GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCTGCTACTCCAGGCTAACCTGAACTCCCC  
ATGTGATGCGCGCTTTGTTGAATGTGTGTCTCGGTTTCCCCATCTGTAATATGAGTCGGGGG  
GAATGGTGGTGATTCTTACCTCACAGGGCTGTTGTGGGGATTAAAGTGCTGCGGGTGAGTGA  
AGGACACATCACGTTCAAGTGTTCAGTACAGGCCACAAAACGGGGCACGGCAGGCCTGAG  
CTCAGAGCTGCTGCACTGGGCTTTGGATTTGTTCTTGTGAGTAAATAAACTGGCTGGTGAA  
TGA

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**FIGURE 167**

MFLLLPFDSLIVNLLGISLTVLFTLLLVFIIIVPAIFGVVSFGIRKLYMKSLLKIFAWATLRME  
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRS GSSKALDNTPEFELSDIFYFCRKGME  
TIMDDEVTKRFSAAEELSWNLLSRTNYNFQYISLRLTVLWGLGVLIRYCFLLPLRIALFTG  
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRPNGGICVANH  
TSPIDVIILASDGYAMVGQVHGGLMGVIQRAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ  
DKSKLPILIFPEGTCINNTSVMFMFKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMVTYL  
LRMMTSWAIVCSVWYLPPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKVKDTF  
KEEQQKLYSKMIVGNHKDRSRS

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**FIGURE 168**

CCCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCCGCCCTCACCCGGACCCCTGGCCCTCA  
CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC  
ACCTGGCAGGCCAGGCTGTCCCCACCATCCTGCCCCCTGGGCCTGGCTCCAGACACCTTTGA  
CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG  
AAATGGCCCCACCATGCCCTGCTGCGGGAATCCTGGGAGGCAGCCAGGAGACCTGGGAGGAC  
AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT  
CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG  
GCTCCCGGGAGCTCTACATGAGGCACTTTCCTTCAAGGCCCTGCATTTCTACCTGATCCGG  
GCCCTGCAGCTGCTGCGAGGCAGTGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCGG  
AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT  
TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCACAGATTTGGGGAGAAGAGGCGGGGCTGT  
GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTTGCCCCCTG  
GAAGACTCTGCTCTTGCCCCCTGGAGAGTTCCAGCTCTCAGGGGTTGGGCCCTGAAAGTCCA  
ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG  
CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCAGG  
ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGGACTTCCT  
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGTGCAATGTGGAGACA  
TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

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**FIGURE 169**

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH  
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSNTLYWELNQAVRTGGGSREL  
YMRHFPFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS  
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP



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**FIGURE 170**

GTGGCTTCATTTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA  
CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG  
GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC  
TATTGTCTGGACCTTCAACACAACCCCTCTTGTACCATAACAGCCAGAAGGGGGCACTATCA  
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG  
CTCAGCAAATGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT  
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG  
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG  
GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC  
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT  
GCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT  
GAAGGTGCTGCTGATGACCCAGATTCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGCCCT  
CCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTCTGAAGAGAGAGAGACAAGAAG  
AGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCGGGAACTCCTAACATATGCCCCCAT  
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA  
TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC  
TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATCTTAGACAGCAGTG  
CACTCCCCTAAGTCTCTGCTCA

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**FIGURE 171**

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT  
IQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV  
YEHLSPKVTMGLQSNKNGTCVTNLTCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW  
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW  
FLKRERQEEYIEEKKRVDICRETPNICPHSGENTYDTIPHTNRTILKEDPANTVYSTVEIP  
KKMENPHSLLTMPDTPRLFAYENVI

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**FIGURE 172**

CTGGTTCCCCAACATGCCTCACCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC  
TCTGGACCCCGTGAAAGAGCTGGTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC  
CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACAACCCCTCTTGTCAACCATAC  
AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA  
GATGGAGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT  
GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG  
AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG  
ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT  
GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG  
AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCC  
ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCCTCCATGGTCCTCCT  
GTGTCTCCTGTTGGTGCCCCCTCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTC  
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCGGGAA  
ACTCCTAACATATGCCCCCATTTCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA  
TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA  
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG  
AATGTTATCTAGACAGCAGTGCCTCCCCCTAAGTCTCTGCTCAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 173**

GAAAGACGTGGTCCTGACAGACAGACAATCCTATTCCCTACCAAAATGAAGATGCTGCTGCT  
GCTGTGTTTGGGACTGACCCTAGTCTGTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA  
ACTTTAATGTAGAAAAGATTAATGGGGAATGGCATACTATTATCCTGGCCTCTGACAAAAGA  
GAAAAGATAGAAGAACATGGCAACTTTAGACTTTTTCTGGAGCAAATCCATGTCTTGGAGAA  
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTTG  
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTTACT  
ATACCTAAGACAGACTATGATAACTTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGGA  
AACCTTCCAGCTGATGGGGCTCTATGGCCGAGAACCAGATTTGAGTTCAGACATCAAGGAAA  
GGTTTGCACAACTATGTGAGGAGCATGGAATCCTTAGAGAAAATATCATTGACCTATCCAAT  
GCCAATCGCTGCCTCCAGGCCCAGAAATGAAGAATGGCCTGAGCCTCCAGTGTTGAGTGAGAC  
ACTTCTCACCAGGACTCCACCATCATCCCTTCCTATCCATACAGCATCCCCAGTATAAATTC  
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCCAGTCTATCAACATGTTACC  
TAGGATACCTCATCAAGAATCAAAGACTTCTTTAAATTTCTCTTTGATACACCCTTGACAAT  
TTTTCATGAAATTATTCCCTCTTCCTGTTCAATAAATGATTACCCTTGCACTTAA

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**FIGURE 174**

MKMLLLLCLGLTLCVHAEEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ  
IHVLENSLVLVKVTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI  
NEKDGETFQLMGLYGREPDLSSDIKERFAQLCEEHGILRENIIDLSNANRCLQARE

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**FIGURE 175**

GGCTCGAGCGTTTCTGAGCCAGGGGTGACCATGACCTGCTGCGAAGGATGGACATCCTGCAA  
TGGATTGAGCCTGCTGGTTCTACTGCTGTTAGGAGTAGTTCTCAATGCGATACCTCTAATTG  
TCAGCTTAGTTGAGGAAGACCAATTTTCTCAAACCCCATCTCTTGCTTTGAGTGGTGGTTC  
CCAGGAATTATAGGAGCAGGTCTGATGGCCATTCCAGCAACAACAATGTCCTTGACAGCAAG  
AAAAAGAGCGTGCTGCAACAACAGAACTGGAATGTTTCTTTCATCATTTTTTCAGTGTGATCA  
CAGTCATTGGTGCTCTGTATTGCATGCTGATATCCATCCAGGCTCTCTTAAAAGGTCCTCTC  
ATGTGTAATTCTCCAAGCAACAGTAATGCCAATTGTGAATTTTCATTGAAAAACATCAGTGA  
CATTCATCCAGAATCCTTCAACTTGCAGTGGTTTTTCAATGACTCTTGTGCACCTCCTACTG  
GTTTCAATAAACCCACCAGTAACGACACCATGGCGAGTGGCTGGAGAGCÂCTAGTTTCCAC  
TTCGATTCTGAAGAAAACAAACATAGGCTTATCCACTTCTCAGTATTTTATAGGTCTATTGCT  
TGTTGGAATTCTGGAGGTCCTGTTTGGGCTCAGTCAGATAGTCATCGGTTTCCTTGGCTGTC  
TGTGTGGAGTCTCTAAGCGAAGAAGTCAAATTGTGTAGTTTAATGGGAATAAAATGTAAGTA  
TCAGTAGTTTGAAAAAAAAAAAA

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**FIGURE 176**

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA  
IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA  
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDEENKHRL  
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

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**FIGURE 177**

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGAGGCT  
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT  
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC  
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG  
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAATTAGTGAA  
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC  
CTGATCTTCACTAAAAATTGTAAAGGTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC



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**FIGURE 178**

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV  
KHCTDQISFKKRLSLKKSWWK

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**FIGURE 179**

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGG  
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG  
GAGCAGATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCTCTCCCCCTGCAGCCCTGCCCTC  
GAACTGTGACATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGG  
AAGCCAATGACCCATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAG  
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGG  
CAAATGCAAATACAAGAGCAGCCAGAAGCAGCACAGTCCTGTACCTGAGAAGGCCATCCCAC  
TCATCACTCCAGGCTCTGCCACTACTTGCTTGAGCACAGGACTGGCCTCCAGGGATGGCCTGA  
AGCCTAACACTGGCCCCCAGCACCTCCTCCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTC  
TCTCCAAGGGCAGGCTGTTAGGCCCTTTCTGATCAGGAGGCTTCTTTATGAATTAACTCG  
CCCCACCACCCCCTCA

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**FIGURE 180**

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAGIAAVLSGKCK  
YKSSQKQHSPVPEKAIPLITPGSATTC

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**FIGURE 181**

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGG**ATG**TCGCTGCTGAGCCTGCCC  
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC  
CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACCTGCCGCCGGCTCC  
AGTGTTTCCACAGCCCCCAAACGGAACCTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT  
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTGCGCCACCTATTCCCAGGGCTTTACGGT  
ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA  
CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCTGAAGCCCTGG  
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC  
GCCCCGCTTCCATTTCAACATCCTGAAGTCCATATAACGATCTTCAACAAGAGTGCAAACA  
TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG  
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG  
TCAGGAGAGGCCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGTAGAGAAAA  
GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGGCGGCGC  
TTCCACAGGGCCTGCCGCCTGGTGCATGACTTCACAGACGCTGTCATCCGGGAGCGGCGTCG  
CACCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG  
ATTTCAATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT  
ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGGCCTCTC  
CTGGGTCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC  
AAGAGCTTCTGAAGGACCGCGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC  
TTCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG  
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC  
TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC  
CCCTTCGCTTTGACCCAGAGAACAGCAAGGGGAGGTACCTCTGGCTTTTATTCTTTCTC  
CGCAGGGCCCAGGAACTGCATCGGGCAGGCGTTCGCCATGGCGGAGATGAAAGTGGTCCTGG  
CGTTGATGCTGCTGCACTTCGGTTCCCTGCCAGACCACACTGAGCCCCGAGGAAGCTGGAA  
TTGATCATGCGCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCTGAATGTAGGCTTGCA  
**GTGA**CTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAA

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**FIGURE 182**

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPPQPPKRNWFWG  
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF  
IRFLKPWLGEKILLSGGDKWSRHRRLTPAFHFNILKSYITIFNKSANIMLDKWQHLLASEGS  
SRLDMFEHISLMTLDSLQKCFSDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY  
LSHDGRRFHRACRLVHDFTDAVIRERRRTLPTQGIDDFKDKAKSKTLDLFDVLLLSKDEDG  
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEW  
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW  
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT  
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

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**FIGURE 183**

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATCATGTATAAGCTGGCCTCCTGC  
TGTTTGCTTTTCACAGGATTCTTAAATCCTCTCTTATCTCTTCCTCTCCTTGACTCCAGGGA  
AATATCCTTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACTCCGGAGGAGCTAGAAA  
GAGCTTCCCTTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG  
AAAGCAGACTCAAGTACCAACATTTTTAAACCAAGAGGAAATTTGAGAAAGTTTCAGGATTT  
CTCTGGACAAGATCCTAACATTTTACTGAGTCATCTTTGGCCAGAATCTGGAAACCATACA  
AGAAACGTGAGACTCCTGATTGCTTCTGGAAATACTGTGTCTGAAGTGAAATAAGCATCTGT  
TAGTCAGCTCAGAAACACCCATCTTAGAATATGAAAAATAACACAATGCTTGATTTGAAAAC  
AGTGTGGAGAAAACTAGGCAAACCTACACCCTGTTTATTGTTACCTGGAAAATAAATCCTCT  
ATGTTTTGCACAAAAA

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**FIGURE 184**

MYKLASCCLFTGFLNPLLSLPLDSREISFQLSAPHEDARLTPEELERASLLQILPEMLGA  
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

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**FIGURE 185**

GAACATTTTTAGTTCCCAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGGAT  
GGGGTTGCTGGTTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA  
CCACCTCCGCCAGGAAGTGCAGGCCCCACCTGTCTGCAACCCAGCTGAGGCCATGCCCTCCCC  
AGGGACCGTCTGCAGCCTCCTGCTCCTCGGCATGCTCTGGCTGGACTTGGCCATGGCAGGCT  
CCAGCTTCCTGAGCCCTGAACACCAGAGAGTCCAGCAGAGAAAGGAGTCGAAGAAGCCACCA  
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCCCGGAAGATGGAGGTCAAGCAGA  
AGGGGCAGAGGATGAACTGGAAGTCCGGTTCAACGCCCCCTTTGATGTTGGAATCAAGCTGT  
CAGGGGTTTCAGTACCAGCAGCACAGCCAGGCCCTGGGGAAGTTTCTTCAGGACATCCTCTGG  
GAAGAGGCCAAAGAGGCCCCAGCCGACAAGTGATCGCCCACAAGCCTTACTCACCTCTCTCT  
AAGTTTAGAAGCGCTCATCTGGCTTTTCGCTTGCTTCTGCAGCAACTCCCACGACTGTTGTA  
CAAGCTCAGGAGGCGAATAAATGTTCAAAGTGTGTA



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**FIGURE 186**

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG  
GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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**FIGURE 187**

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCTCGTCCAGTACCTC  
GTGAACCCCGGGGTGCTCCGCACGGACCCAGATGTCAAGAAT**ATGA**ACACGTGGCTGCTGT  
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG  
CTCCTGCTGGACTTTCTTGGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT  
GAGTATGTCCCCACCCCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC  
TTACACCTCTACTTGAGTATGTCCCTAACCTGAGCCCCCACGCCTGGGGCCAGAGTCTTT  
GTCCCCCGTGTGCGCATGTGTTTCAGGGTCAGCCTCTCCCAGAAGTGAGATCATGGACAAAAA  
GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCAGCAAGAAGCTGAAC  
TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCT**TGA**AGTAACAAGTTTAAATGTTTCTCAGA  
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT  
CCAAAAACACAAGTAGAAATTCTAACAATGAAATATATTACAGGCAGGTACCCACTAACCA  
AACAACCTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC  
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT  
AACAACAACCTCCCTGCTCCTGGCACCAGCCGTTTTGGTCATGGTGGGCCAGCTGCAAAGCG  
TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC  
ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA  
ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTGAGGCTCTGGGCTCACCTCCATCTCCAGA  
GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCAGCTCAGAATGAACACACCCACCAAGA  
GCCTCCTTGTTTATAACACAGGTTACCCTACAAACCACTGTCCCCACACAACCCTGGGGAT  
GTTTTTAAACACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCTGAGGGTTGA  
ATTTTTTTTAAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 188**

MNTWLLFLPLFPVQVQTLIVVVIIGMLVLLLDLGLVHLGQLLI FHIYLSMSPTLSPRSPQGW  
VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ  
AQQEAELTPRPAGVVPGA

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**FIGURE 189**

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAGCTGCAAGACGCTGACCATGGCCAAG  
ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT  
ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG  
TGCCCAAGCCCCTGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG  
GATGGAGATAACCAACACATCCACCCAGGAGGTGGTACAATAACAAGTGGGAGACTGGGGATGA  
CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAACTGTGGAAG  
AACCAGGGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA  
GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA  
GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTCCCCTGGGGCTTTGTGGCAAAAATCCTA  
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT  
ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAAGTGAAGCGCCTTTGCTG  
CTGTTTCCTCTGTCCTGTCAGGTCTCCTGGGGATGGTGGCCACATGATGTATTACAAAGTC  
TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGAATTATGGCTG  
GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA  
ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCATAGTAAGAGCTTCAAGGAAAAC  
CCGAAGTGCCTACCACATCACCATCAGTGTTTCCCTCGGCGGCTGTCAAGTGCAGCCCCCAC  
CGTGGGTCCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG  
GAGTCGACTTCTACTCCGAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTG  
AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA  
GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG  
TCTCTTGAGCATGGTTTTTtagaggctacgaataaggctatgaataagggttatctttaagtc  
ctaagggattcctgggtgccaactgctctcttttctctacagctccatcttgtttcaccac  
cccacatctcacacatccagaattcccttctttactgatatgttctgtgccagggttctgggc  
taaaccatggagataaaaagaagagtaaaatacacttccccgaccttaaggatctgaaa

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**FIGURE 190**

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP  
VSLDGD TNTSTQE VVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR  
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPLGLCGKNPMVIPGNADHLHRTSIHQL  
PPATNRLATHWEPC LWAQTERLCCCFLCPVRSPGDGGPHDVFTSLP SDCQLGSRRL ETTCLE  
LWLGLLHGLALLHLLHGVGCHHLQHVVHQDGAGVQVQA

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**FIGURE 191**

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAGATGTGGTTACCCCTTGGTCTCCTG  
TCTTTATGTCTTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA  
GCAGCTCCTGTGGACATTGCCATCCCCTCTGGTAGCCTTCAGAGCAAACAGGACAACCTATG  
TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT  
GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG  
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAATCTTGCCTGCCCTATTCCTCCTCCCAA  
GTCTGTTCTCTTATTGTCAACCTCAGCACAAACAGGCTGGCGCCAATGGCATTACAGAGAAAG  
CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT  
AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCTTCCCCCTGCCCGCCGTAGATTCAG  
GACATTGCCCCCTGTGTGCCACCAAACCAGGACTTCCCCTTGGCTTGGCATCCCTGGCTCT  
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT  
ATGGCGATGGCCATGATGTTACAATCCCCTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA  
GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCTGAGGAAAAACCAA  
GGGAAGCAACAGGAACCTCTGCAACTGGTTTTTATCGGAAAGATCATCCTGCCTGCAGATGC  
TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA  
ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAACTCTTTATTACTTTGGG  
AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG  
AACCAAGGAACTAACAAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC  
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

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**FIGURE 192**

MWLPLGLLSLCLSPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQSGME  
HRNHLCFCDLYDRATSPPLKCSLL

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**FIGURE 193**

GTAGCGCGTCTTGGGTCTCCCGGCTGCCGCTGCTGCCGCCGCCGCTCGGGTCGTGGAGCCAGGAGCGACGTCA  
CCGCCATGGCAGGCATCAAAGCTTTGATTAGTTTGTCTTTGGAGGAGCAATCGGACTGATGTTTTTGATGCTT  
GGATGTGCCCTTCCAATATACAACAAATACTGGCCCCCTTTGTTCTATTTTTTACATCCTTTCACCTATTCC  
ATACTGCATAGCAAGAAGATTAGTGGATGATACAGATGCTATGAGTAACGCTTGTAAAGGAACTTGCCATCTTTC  
TTACAACGGGCATTGTCTGTCTCAGCTTTTGGACTCCCTATTGTATTTGCCAGAGCACATCTGATTGAGTGGGGA  
GCTTGTGCACTTGTCTCACAGGAAACACAGTCATCTTGCAACTATACTAGGCTTTTTCTTGGTCTTTGGAAG  
CAATGACGACTTCAGCTGGCAGCAGTGGTGAAGAAATTAAGTGAATATTGTCAAATGGACTTCCTGTCAATTT  
GTTGGCCATTACGCACACAGGAGATGGGGCAGTTAATGCTGAATGGTATAGCAAGCCTCTTGGGGGTATTTTA  
GGTGTCCCTTCTCACTTTTATTGTAAGCATACTATTTTCACAGAGACTTGCTGAAGGATTAAAGGATTTTCT  
CTTTTGGAAAAGCTTGACTGATTTTCACACTTATCTATAGTATGCTTTTTGTGGTGTCTGCTGAATTTAAATAT  
TTATGTGTTTTCTGTTAGGTTGATTTTTTTTGGAAATCAATATGCAATGTTAAACACTTTTTTAATGTAATCA  
TTTGCATTGGTTAGGAATTCAGAATTCGGCCGGCTCTATTACTGGTCAAGTACATCTTTTCTCTTAAATATTAT  
TAGCCTCCATTATTACAAAAAATTATAAAAAATAAGTTTCAGTCAGTCAGGATGACATCACTCCCAATGTTATG  
CAGACATACAGACGGTTGGCATACTGTATAGTGTACTCAGTGCAAATATAGCTGCATTTATACCTCAGAG  
GGGCCAAGTGTTAATGCCCAGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTG  
AAAATTATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTCTCAATTGTTAGAAGAATTTATGTTAAACTTTA  
AGGTAAGGGTGTA AAAACATTTTTGAGATAAGGTTTTTATTATGTTTATTATTGTTAGAGTGAGTTGCAATGT  
GGGAAGAAATGACATTGAAATTCAGTTTTTGAATCCTGTTTCTATTTATAAGTGAAATTTGTGATCTCCTATC  
AACCTTTCATGTTTTACCCTGTTAAATGGACATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTTGC  
ATCATATATGCCAGAAAACCTTCCTCTGCTTCCCTCTTTTGACTTATTTGGTATGTTGTATATATTACATAAAA  
TAACCTTTCAAATATAGTTTAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTACATT  
CAGAGTGCCCCCTCCCCTGCAAGGCCTTGCCATGATTAACAAGTAACTTGTTAGTCTTACAGATAATTCATGCA  
TTAACAGTTTAAGATTTAGACCATGGTAATAGTAGTCTTATTCTCTAAGGTTATATCATATGTAATTTAAAG  
TATTTTTAAGACAAGTTTCCGTGTATACCTCTGAAGTGTGTTGATTTTGAGTTCATCATGATAGATCTGCTGTTT  
CCTTATAAAAAGGCATTTGTTGTGTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACAT  
ACCTGACCAAAAAAATCCCAGTAACCAAGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAGGA  
CTTTTTTCAGGAGTGGGTATATAAAAAACATTCAGTTGGTCTGACAGTATTTTGTAAAGGATATTTGTTTGTATG  
TTTATTCAGTATACTTACATAAAAAATTTTTCGCCATCAGCCAAAACCTCAGTAATCATGACAGCTGTCTGTTGT  
TTTATGAAGTTTATTTCTCAAGAAAATGGGAATAAATTTGGGATTTGTTTCAGCTTTTTTACTAAAGATGCCTAA  
AGCCACAGGTTTTATTGCCCTAACTTAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCG  
GCGTGTGGCTGGAGCCTTCCCACTGGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTTCAGATTTCAAGAGGAA  
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACCTCTTGTGCTTGTGATCTACTGGACTTT  
TTTTTTGCAGGAAGTGCATTCTCTGGTCTTCCCTATTTTCTGTTCTGGATGTCAGTGCACTGCACTGCTACTG  
TTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGCGTATTATTTCTATATACTAATTGCATTGGCAGCATT  
GTGCTTTGACCTTGTATACTAGCTTGACATAGTGTCTCTGATTTCTAGGCTAGTTACTTGAGATATGAAT  
TTTCCATAGAATATGCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACCTTTTGATGATGAAACAATAA  
AGATTTTAAATATCTATTTTAAAAA



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**FIGURE 194**

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM  
SNACKELAIFLTGTGIVVSAFGLPIVFARAHLEWGACALVLTGNTVIFATILGFFLVFGSND  
DFSWQQW

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**FIGURE 195**

CCCACGCGTCCGCCCCACGCGTCCGCCCCACGCGTCCGCCCCACGCGTCCGCCCCACGCGTCCGCGC  
CACGCGTCCGCGTGCAGCTCGCGCCGCACACTGCCTGGTGGAGGGAAGGAGCCCGGGCGCTCTCGCCGCTCCC  
CGCGCCGCGCTCCGCACCTCCCCACCGCCCGCGCCCGCCCGCCCGCCGCAAGCATGAGTGAGCCCGCTC  
TCTGCAGCTGCCCGGGGCGGAATGGCAGGCTGTTTCCGCGGAGTAAAGGTGGCGCCGCTCAGTGGTTCGTTT  
CAATGACGGACATTAACAGACTGTCAGATCCTGGGGAGTGCAGACCCCGAGTTTGGAGTTTTTCCCCC  
AACGTCACAGTCCGAAGTGCAGAGGGAAGGAAGGCGGAGGGAAGGCGAAGCTCGGGCTCCGGCACGTAGTTGG  
GAACTTGGGGTCTAGAAGTCGCCTCCCCGCCTTGCCGGCCGCCCTTGACGCCCCGAGCCGAGCAGCAAAGT  
GAGACATTGTGCGCCTGCCAGATCCGCCGGCCGCGGACCGGGCTGCCTCGGAAACACAGAGGGGTCTTCTCTC  
GCCCTGCATATAATTAGCTGCACACAAAGGGAGCAGCTGAATGGAGTTGTCACTCTCTGGAAAAGGATTTCT  
GACCGAGCGCTTCCAATGGACATTCTCCAGTCTCTCTGGAAAGATTCTCGCTAATGGATTCTGCTGCTCGGT  
CTCTGTCTATACTGGCTGCTGAGGAGGCCCTCGGGGGTGGTCTTGTGTCTGCTGGGGGCTGCTTTTCAATGCT  
GCCCGCCGCCCCAGCGGGTGCCCGCAGCTGTGCCGGTGCGAGGGGCGGCTGCTGTACTGCGAGGCGCTCAACC  
TCACCGAGGCGCCCCACAACCTGTCCGGCTGCTGGGCTTGTCCCTGCGCTACAACAGCCTCTCGGAGCTGCGC  
GCCGGCCAGTTTACGGGGTTAATGCAGCTCACGTGGCTCTATCTGGATCACAATCACATCTGCTCGGTGCAAGG  
GGAGCCCTTTCAGAACTGCGCCGAGTTAAGGAAGTACGCTGAGTTCCAACAGATCACCAACAGATCCCCAAC  
CCACCTTCCGGCCCATGCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTGCAGGCGCTCGCGCCCGAC  
CTCTTCCACGGGCTGCGGAAGCTCACACGCTGCATATGCGGGCCAAACGCCATCCAGTTTGTGCCCGTGCGCAT  
CTTCCAGGACTGCCGAGCCTCAAGTTTCTCGACATCGGATACAATCAGCTCAAGAGTCTGGCGCGCAACTCTT  
TCGCGGGCTTGTAAAGCTCACCGAGCTGCACCTCGAGCACAACGACTTGGTCAAGGTGAAGTTTCCGCCACTTC  
CCGCGCCTCATCTCCCTGCACTCGCTCTGCCTGCGGAGGAACAAGGTGGCCATTGTGGTCACTCGCTGGACTG  
GGTTTGGAACTGGAGAAAATGGACTGTGCGGGCAACGAGATCGAGTACATGGAGCCCATCTGGCGCGCAACTCT  
TGCCGCACTGCACTCCCTGCACTGCACTGCACTCCAACCGCTCACCTACATCGAGCCCGGATCCTCAACTCTTG  
AAGTCCCTGACAAGCATCACCTGCGCGGAACCTGTGGGATTGCGGGCGCAACGTGTGTCCTAGCTAGCTCGTG  
GCTCAGCAACTTCCAGGGGCGCTACGATGGCAACTTGCACTGCGCCAGCCCGGAGTACGCACAGGGCGAGGACG  
TCCTGGAGCGCGTGTACGCTTCCACCTGTGCGAGGATGGGGCGGAGCCACCAGCGGCGCCCTGCTCTCGGCC  
GTCAACCAACCGCAGTGATCTGGGGCCCCCTGCCAGCTCGGCCACCAACGCTCGCGGACGGCGGGGAGGCGCA  
CGACGGCACATTGAGCCTGCCACCGTGGCTCTTCCAGGCGCGGAGCAGCGCGGAGAACGCCGTGCAGATCCACA  
AGGTGGTACGGGCGACCATGGCCCTCATCTTCTCTCTCATCGTGGTCTGCTGCTACGTGTCTGGAG  
TGTTTCCAGCCAGCCTCAGGCAGCTCAGACAGTGTCTTGTACGCGAGCGCAGGAAGCAAAAGCAGAAACAGAC  
CATGCATCAGATGGCTGCCATGTCTGCCAGGAATACTACGTTGATTACAACCGAACCACATTGAGGGAGCCC  
TGGTGATCATCAACGAGTATGGCTCGTGTACCTGCCACCAGCAGCCCGGAGGGAAATGCGAGGTGTGATTGTCC  
CAGTGGCTCTCAACCCATGCGCTACCAAATACGCCTGGGCGAGCCGGGACGGGCGGGCGGCGGCGGCGGCTGGGT  
CTCCTTGTCTGTGCTCTGATATGCTCCTTGACTGAACTTTAAGGGGATCTCTCCAGAGACTTGACATTTTAG  
CTTTATTGTCTTAAAAACAAAAGCGAATTAACACACAAAAAACCCACCCACAACTTCAGGACAGTC  
TATCTTAAATTTTATATGAGAATCCTTCCCTCCCTTTGAAGATCTGTCCATATTAGGAATCTGAGAGTGAAA  
AAAGGTGGCCATAAGACAGAGAGAGAATAATCGTGCTTTGTTTTATGCTACTCTCCACCCCTGCCCATGATTA  
AACATCATGTATGTAAGATCTTAAGTCCATACGCACTTATGTAAGAACCATTGGAAGAGGAATCTGCAATC  
TGGGAGCTTAAGAGCAAATGATGACCATAGAAAGCTATGTTCTTACTTTGTGTGTGTGTCTGTATGTTTCTGCG  
TTGTGTGTCTTTGTAGGCAAGCAACGTTGTCTACACAAACGGGAATTTAGCTCACATCATTTTATGCCCTGT  
GCCTCTAGCTCTGGAGATTGGTGGGGGGAGGTGGGGGAAACGGCAGGAATAAGGGAAGTGGTAGTTTTAACT  
AAGGTTTTGTAACACTTGAATCTTTTCTTCTCAAATTAATTATCTTTAAGCTTCAAGAACTTGCTCTGACC  
CCTCTAAGCAAATACTAAGCATTTAAAGAGAAATCTAATTTTAAAGGTGTAGCACCTTTTTTTTTTATTCTTC  
CCACAGAGGGTGCTAATCTCATTATGCTGTGCTATCTGAAAAGAACTTAAGGCCACAATTACGCTCTCGTCTG  
GGCATTGTGATGGATTGACCTCCATTGTCAGTACCTTCCAGCTGATTAAAGTTCAGCAGTGGTATTGAGGTT  
TTTTCGAATATTTATATAGAAAAAAGTCTTTTTCATGACAAATGACACTCTCACACCAGTCTTAGCCCTAGTA  
GTTTTTTAGGTTGGACCAGAGGAAGCAGGTTAAATGAGACCTGTCTCTGCTGCACTCAGAAAAAATAGGCAGT  
CCCTGATGCTCAGATCTTAGCCTGATATTAATAGTTGAGACCACCTACCCACAATGCAGCCTATACTCCCAAG  
ACTACAAAGTTACCATCGCAAAGGAAAGGTTATTCAGTAAAAGGAATAGTTTCTCAACCATTTAAAAATAT  
TCTTCTGAACTCATCAAAGTAGAAGAGCCCCAACCTTTTCTCTGCTTCAAGAAGGCAGACATTTGGTATG  
ATTTAGCATCAACAACACATTTATGAGTATATGTAAGTAATCAGAGGGGCAATGCCACTTGTATTCTCCCA  
AGTTTTCCAAGCAAGTACACACAGATCTCTGGTAGGATTAGGGGCCACTTGTGTTTCCGGCTATTTTAGTCTGA  
CTTGTGCAAGTTTGTATGCTTAGTCTATCTGACATGGCCAGTAGAACAGGGCATTGATGGATCACATGAGAT  
GGTAGAAGGAACATCATCACATACCCCTCTCACAGAGAAAATATCAAAGAACCAGAAATATATCTGTTTGG  
AGCAAGAGTGTACATAATGTTTCAGGGTAGTCAAAATAAACATAAATTATCTCTCTAGATGAGTGGCGATGTTG  
GCTGATTTGGGTCTGCCATTGACAGAATGTCAAATAAAAAGGAATTAGCTAGAATATGACCATTAATGTGCTT  
CTGAAATATATTTTGAATAGGTTTGAATGTCA

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**FIGURE 196**

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH  
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNNHICSVQGDAFQKLRRVKELTLSSNQ  
ITQLPNTTFRPMPNLRSDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS  
LKFLDIGYNQLKSLARNSFAGLFKLTEHLEHNDLVKVNFAHFPRILSLHSLCLRRNKVAIV  
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLSIT  
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGAEPTSG  
HLLSAVTNRSDLGPPASSATTLADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA  
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH  
IEGALVIINEYGSTCHQQPARECEV

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**FIGURE 197**

GTGCAAGGAGCCGAGGCGAGATGGGCGTCCTGGGCCGGGTCCTGCTGTGGCTGCAGCTCTGC  
GCACTGACCCAGGCGGTCTCCAAACTCTGGGTCCCCAACACGGACTTCGACGTCGCAGCCAA  
CTGGAGCCAGAACCGGACCCCGTGCGCCGGCGGGCGCCGTTGAGTTCCCGGCGGACAAGATGG  
TGTCAGTCCTGGTGCAAGAAGGTCACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGGAA  
CTCGTCCTGGCTTCAGGAGCCGGATTTCGGCGTCTCAGACGTGGGCTCGCACCTGGACTGTGG  
CGCGGGCGAACCTGCCGTCTTCCGCGACTCTGACCGCTTCTCCTGGCATGACCCGCACCTGT  
GGCGCTCTGGGGACGAGGCACCTGGCCTCTTCTTCGTGGACGCCGAGCGCGTGCCCTGCCGC  
CACGACGACGTCTTCTTTCCGCCTAGTGCCTCCTTCCGCGTGGGGCTCGGCCCTGGCGCTAG  
CCCCGTGCGTGTCCGCAGCATCTCGGCTCTGGGCCGGACGTTACGCGCGACGAGGACCTGG  
CTGTTTTCTGGCGTCCCGCGCGGGCCGCCTACGCTTCCACGGGCCGGGCGCGCTTGAGCGTG  
GGCCCCGAGGACTGCGCGGACCCGTCTGGGCTGCGTCTGCGGCAACGCGGAGGCGCAGCCGTG  
GATCTGCGCGGCCCTGCTCCAGCCCCT

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**FIGURE 198**

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE  
GHAUSDMLLPLDGELVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRSRSGDEA  
PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPGASPVVRVRSISALGRTFTRDEDLAVFLASR  
AGRLRFHGPGLSVGPEDCADPSGCVCGNAEAQPWICAALLQP



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**FIGURE 200**

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP  
FARDAVKKCFVCLA

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**FIGURE 201**

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCCCTCCAGTCACCCTCCCGCCGTTACCCGCGGCGCGC  
CCGAGGGAGTCTCCTCCAGACCCTCCCTCCCGTTGCTCCAACTAATACGGACTGAACGGATCGCTGCGAGGGT  
GGGAGAGAAAATTAGGGGGAGAAAGGACAGAGAGAGCAACTACCATCCATAGCCAGATAGATTATCTTACACTG  
AACTGATCAAGTACTTTGAAAATGACTTCGAAATTTATCTTGGTGTCTTCATACTTGCTGCACTGAGTCTTTC  
AACCACCTTTTCTCTCCAAGTACAGCCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACT  
TATATAAAGTTCCAACGCCCCATTTTCATTATATTATGAAATATGGTGTTCACGTGAAGCAAGTTACTAATGTT  
TTTATTACAAAACCTACCCTAACCATTTACTTTGGTAACTGGCCTCTTTCAGAGAAATCATGGGATTGTTGC  
AAATGATATGTTTGATCCTATTCGGAAACAAATCTTCTCCTTGGATCACATGAATATTTATGATTCCAAGTTT  
GGGAAGAAGCGACACCAATATGGATCACAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCCGA  
ACAGATGTAAAAATACATAAGCGCTTTCCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAG  
AGTTGCCAAAATTGTTGAATGGTTTACGTCAAAAGAGCCCAATAATCTTGGTCTTCTCTATTGGGAAGACCCTG  
ATGACATGGGCCACCATTTGGGACCTGACAGTCCGCTCATGGGCGCTGTCTTTCAGATATTGACAAGAAGTTA  
GGATATCTCATACAAATGCTGAAAAGGCAAGTTGTGGAACTCTGAACCTAATCATCACAAGTGATCATGG  
AATGACGCACTGCTCTGAGGAAAGGTTAATAGAAGTTGACCACTACCTGGATAAAGACCACTATACCCTGATTG  
ATCAATCTCCAGTAGCAGCCATCTTGCCAAAAGAGGTAATTTGATGAAGTCTATGAAGCACTAACTCAGCT  
CATCCTAATCTTACTGTTTACAAAAAAGAACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCGAATTC  
ACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATGACTTTCTGTTAGGCAACC  
ACGGTTACGATAATGCGTTAGCAGATATGCATCCAATATTTTAGCCCATGGTCTGCCTTCAGAAAGAATTC  
TCAAAGAAGCCATGAAGTCCACAGATTTGTACCCACTACTATGCCACCTCCTCAATATCACTGCCATGCCACA  
CAATGGATCATTCTGGAATGTCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTA  
CTATACTCCTCCCTGGTAGTGTAAACCAGCAGAATATGACCAAGAGGGGTCAATACCCTTATTTATAGGGGTC  
TCTCTTGGCAGCATTATAGTGATTGTATTTTTGTAAATTTTCATTAAGCATTTAATTCACAGTCAAATACCTGC  
CTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCCTAATGTTACTTTGAAGTGGATTGTCATA  
TTGAAGTGGAGATTCCATAATTATGTCAGTGTTTAAAGGTTCAAATTCCTGGGAAACCAGTTCCAAACATCTGC  
AGAAACCATTAAGCAGTTACATATTTAGGTATACACACACACACACACACATACACACACACGGACCAAA  
ATACTTACACCTGCAAAGGAATAAAGATGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATAAG  
ATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATATTTAGCAACTTGCCTATGTAAAGTACCTTATAT  
ATTGCATTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCACTTTATGGACAGTTATGTCTTATAAC  
TTGATTGAAATGACAACCTTTTGCACCCATGTACAGAATACTTGTTACGCATTGTTCAAACCTGAAGGAAATT  
TCTAATAATCCCGAATAATGAACATAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTGA  
AAATTAATGTGATAACCTTTGAACCTTGAATTTTGGAGATGTATTCCCAACAGCAGAATGCACTGTGGGCAT  
TTCTTGCTTATTTCTTCCAGAGAACGTGGTTTTTCATTATTTTTCCCTCAAAAGAGAGTCAAATACTGACAG  
ATTGCTTCTAAATATATTGTTTCTGTCAAAAATTATTGTGATTTCTGATGAGTCATATTACTGTGATTTTCA  
TAATAATGAAGACACCATGAATATACTTTTCTTCTATATAGTTAGCAATGGCCTGAATAGAAGCAACCAGGCA  
CCATCTCAGCAATGTTTTCTCTGTTTGAATTTTGTCTCTTTGAAAATTAAATCACTATTAATTACATTA  
AAATCAAATTGGATAAAAAAAAAAAAAAAAAAAAAA



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**FIGURE 202**

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK  
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEEATPIW  
ITNQ RAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY  
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER  
LIELDQYLDKDHYTLLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN  
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD  
LYPLLCHLLNITAMPNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF  
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

**Signal Peptide:**

amino acids 1-22

**Transmembrane Domain:**

amino acids 429-452

**N-glycosylation sites:**amino acids 101-104, 158-161, 292-295, 329-332, 362-365, 369-  
372, 382-385, 389-392**Somatomedin B Domain:**

amino acids 69-85

**Sulfatase protein Region:**

amino acids 212-241

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**FIGURE 203**

GGATTTTGTGATCCGCGATTTCGCTCCACGGGCGGGACCTTTGTAACTGCGGGAGGCCCAG  
GACAGGCCCCACCCTGCGGGGCGGGAGGCAGCCGGGGTGAGGGAGGTGAAGAAACCAAGACGC  
AGAGAGGCCAAGCCCCTTGCCCTGGGTACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA  
CCAGATCCAGAGGCAACAGGGACATGCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC  
AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA  
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGGAGG  
AGCAGCCACCACCACACCAAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCCTGACGTTGCC  
CCTGCCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAACTGTT  
CAGCTCCACAGGTTTTCAGGTCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTG  
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG  
GTATCCACTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT  
ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG  
TGGTCTCATTATCCTGGACATTGTCTCCTGTTCCAGGAGCACCAAGTTTGAGGCTCTGGGC  
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT  
TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAACAGATGAATGTACAATTGGCCGCCA  
AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCTGGACTGATGAGTTTGCTGTATC  
AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT  
CACACAGCCACCGTGAAAGTCCTGGAGTAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAG  
CAGGCTGGCATGTTCACTGGGCTGGTGTTACGACAGAGAACCTGACAGTCACTGGCCAGTTA  
TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAAGAGAACAAAACC  
AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 204**

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGGDYHAWNINYYKKWENEEEEEEEEQPPPTPV  
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFSSSHRFQVIIICLVVLDALLVLAELIDL  
KIIQPDKNNYAAMVFHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILD  
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLLRKQMNVLAAKIQHLEFS  
CSEKPLD

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**FIGURE 205**

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCGAGTGGAGCACCCAGCAGGCGGCCAACAT  
GCTCTGTCTGTGCCTGTACGTGCCGGTTCATCGGGGAAGCCCAGACCGAGTTCCAGTACTTTG  
AGTCGAAGGGGCTCCCTGCCGAGCTGAAGTCCATTTTCAAGCTCAGTGTCTTCATCCCTCC  
CAGGAATTCTCCACCTACCGCCAGTGAAGCAGAGAAATTGTACAAGCTGGAGATAAGGACCT  
TGATGGGCAGCTAGACTTTGAAGAATTTGTCCATTATCTCCAAGATCATGAGAAGAAGCTGA  
GGCTGGTGTAAAGATTTTGGACAAAAGAATGATGGACGCATTGACGCGCAGGAGATCATG  
CAGTCCCTGCGGGACTTGGGAGTCAAGATATCTGAACAGCAGGCAGAAAAAATTTCTCAAGAG  
CATGGATAAAAACGGCAGATGACCATCGACTGGAACGAGTGGAGAGACTACCACCTCCTCC  
ACCCCGTGGAAAACATCCCCGAGATCATCTCTACTGGAAGCATTCCACGATCTTTGATGTG  
GGTGAGAATCTAACGGTCCCGGATGAGTTCACAGTGGAGGAGAGGCAGACGGGGATGTGGTG  
GAGACACCTGGTGGCAGGAGGTGGGGCAGGGGCGCTATCCAGAACCTGCACGGCCCCCTGG  
ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCTCCCGCAGCAACAACATGGGCATCGTTGGT  
GGCTTCACTCAGATGATTTCGAGAAGGAGGGGCCAGGTCACTCTGGCGGGCAATGGCATCAA  
CGTCCCTCAAAATTGCCCCGAATCAGCCATCAAATTCATGGCCTATGAGCAGATCAAGCGCC  
TTGTTGGTAGTGACCAGGAGACTCTGAGGATTCACGAGAGGCTTGTGGCAGGGTCTTTGGCA  
GGGGCCATCGCCAGAGCAGCATCTACCCAATGGAGGTCTGAAGACCCGGATGGCGCTGCG  
GAAGACAGGGCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCTGGCCAGAGAGGGGG  
TGGCCGCTTCTACAAAGGCTATGTCCCCAACATGCTGGGCATCATCCCTATGCCGGCATC  
GACCTTGCAGTCTACGAGACGCTCAAGAATGCCTGGCTGCAGCACTATGCAGTGAACAGCGC  
GGACCCCGGCGTGTGTTGTGCTCCTGGCCTGTGGCACCATGTCCAGTACCTGTGGCCAGCTGG  
CCAGCTACCCCTGGCCCTAGTCAGGACCCGGATGCAGGCGCAAGCCTCTATTGAGGGCGCT  
CCGGAGGTGACCATGAGCAGCCTCTTCAAACATATCTGCGGACCGAGGGGCGCTTCGGGT  
GTACAGGGGGCTGGCCCCAATTTCATGAAGGTATCCAGCTGTGAGCATCAGTACGTGG  
TCTACGAGAACCTGAAGATCACCTGGGCGTGCAGTTCGCGGTGACGGGGGAGGGCCGCCCG  
GCAGTGGACTCGCTGATCCTGGGCGCAGCCTGGGGTGTGCAGCCATCTCATTCTGTGAATG  
TGCCAACTAAGCTGTCTCGAGCCAAGCTGTGAAAACCTAGACGCACCCGCAGGGAGGGT  
GGGGAGAGCTGGCAGGCCCCAGGGCTTGTCTGCTGACCCAGCAGACCCTCCTGTTGGTTCC  
AGCGAAGACCACAGGCATTCCTTAGGGTCCAGGGTCCAGGCTCCGGGCTCACATGTGTAA  
GGACAGGACATTTTCTGCAGTGCCTGCCAATAGTGAGCTTGGAGCCTGGAGGCGGGCTTAGT  
TCTTCCATTTACCCCTTGCAGCCAGCTGTTGGCCACGGCCCCCTGCCCTCTGGTCTGCCGTGC  
ATCTCCCTGTGCCCTCTTGTGCTGCCTGCTGCTGAGGTAAAGGTGGGAGGAGGGCTACAG  
CCCACATCCCACCCCTCGTCCAATCCCATAATCCATGATGAAAGGTGAGGTACGTTGGCCT  
CCCAGGCCTGACTTCCCAACCTACAGCATTGACGCCAATTTGGCTGTGAAGGAAGAGGAAAG  
GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGGCTCTCGGGCATGCT  
TGGGAGTGCAGGGGGCTCGGGCTGCCTGGCTGGCTGCACAGAAGGCAAGTGTGGGGCTCA  
TGGTGCTCTGAGCTGGCCTGGACCCTGTCAGGATGGGCCCCACCTCAGAACCAAACTCACTG  
TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTTGAGGGCGAAGGGCAGAGCGTTTGT  
GTGTTCTGGGGAGGGAAGGAAAAGGTGTTGGAGGCCTTAATTATGGAAGTTGGGAAAAGGG  
TTTTGTCCAGAAGGACAAGCCGGACAAATGAGCGACTTCTGTGCTTCCAGAGGAAGACGAGG  
GAGCAGGAGCTTGGCTGACTGCTCAGAGTCTGTTCTGACGCCCTGGGGGTTCTGTCCAACC  
CCAGCAGGGGCGCAGCGGGACCAGCCCCACATTCCACTTGTGTCACTGCTTGGAACTTATTT  
ATTTTGTATTTATTTGAACAGAGTTATGTCCTAACTATTTTATAGATTTGTTTAATTAATA  
GCTTGTCAATTTCAAGTTCATTTTTTATTCATATTTATGTTTATGTTGATTGTACCTTCCC  
AAGCCCGCCAGTGGGATGGGAGGAGGAGGAGAAGGGGGGCTTGGGCGCTGCAGTCACAT  
CTGTCCAGAGAAATTCCTTTTGGGACTGGAGGCGAGAAAAGCGGCCAGAAAGGCAGCAGCCCTG  
GCTCCTTTCTTTGGCAGGTGGGGGAAGGGCTTGGCCCCAGCCTTAGGATTTTCAAGGTTTGA  
CTGGGGGCGTGGAGAGAGAGGGAGGAACTCAATAACCTTGAAGGTGGAATCCAGTTATTTCT  
CTGCGCTGCGAGGGTTTCTTTATTTCACTCTTTTCTGAATGTCAAGGCAGTGAGGTGCCTCT  
CACTGTGAATTTGTGGTGGGCGGGGGCTGGAGAGAGGCTGGGGGGCTGGCTCCGCTCCCTCC  
CAGCCTTCTGCTGCCCTTGTCTTAACAATGGCGGCCAAGTGGCGACCTACGGTTGCACCTTCC  
ATTCCACCAGAATGACCTGATGAGGAAATCTTCAATAGGATGCAAAGATCAATGCAAAAATT  
GTTATATATGAACATATAACTGGAGTCGTCAAAAAGCAAATTAAGAAAGAATTGGACGTTAG  
AAGTTGTCAATTAAGCAGCCTTCTAATAAAGTTGTTTCAAAGCTGAAAAAATAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 206**

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD  
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEKILK  
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTPDEFTVEERQTGMW  
WRHLVAGGGAGAVSRTCTAPLDRCLKVLMQVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI  
NVLKIAPESAIFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMAL  
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNWLQHYAVNS  
ADPGVFVLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG  
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

**Important features:****Signal peptide:**

amino acids 1-16

**Transmembrane domain:**

amino acids 284-304, 339-360, 376-394

**Mitochondrial energy transfer proteins signature.**

amino acids 206-215, 300-309

**N-glycosylation site.**

amino acids 129-133, 169-173

**Elongation Factor-hand calcium-binding protein.**

amino acids 54-73, 85-104, 121-140

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**FIGURE 207**

GGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATACGCTGGGAACCTTCCCCAGCCAT  
GGCTTCCCTGGGGCAGATCCTCTTCTGGAGCATAATTAGCATCATCATTATTCTGGCTGGAG  
CAATTGCACTCATCATTGGCTTTGGTATTTTCAGGGAGACACTCCATCACAGTCACTACTGTC  
GCCTCAGCTGGGAACATTGGGGAGGATGGAATCCTGAGCTGCACTTTTGAACCTGACATCAA  
ACTTTCTGATATCGTGATACAATGGCTGAAGGAAGGTGTTTTAGGCTTGGTCCATGAGTTCA  
AAGAAGGCAAAGATGAGCTGTCGGAGCAGGATGAAATGTTTCAGAGGCCGGACAGCAGTGTTT  
GCTGATCAAGTGATAGTTGGCAATGCCTCTTTGCGGCTGAAAAACGTGCAACTCACAGATGC  
TGGCACCTACAAATGTTATATCATCACTTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATA  
AAACTGGAGCCTTCAGCATGCCGGAAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTG  
CGGTGTGAGGCTCCCCGATGGTTCCCCCAGCCCACAGTGGTCTGGGCATCCCAAGTTGACCA  
GGGAGCCAACCTTCTCGGAAGTCTCCAATACCAGCTTTGAGCTGAACTCTGAGAATGTGACCA  
TGAAGGTTGTGTCTGTGCTCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAA  
AATGACATTGCCAAAGCAACAGGGGATATCAAAGTGACAGAATCGGAGATCAAAGGCGGAG  
TCACCTACAGCTGCTAAACTCAAAGGCTTCTCTGTGTGTCTCTTCTTTCTTTGCCATCAGCT  
GGGCACTTCTGCCTCTCAGCCCTTACCTGATGCTAAAATAATGTGCCTTGGCCACAAAAAAG  
CATGCAAAGTCATTGTTACAACAGGGATCTACAGAACTATTTACCACCAGATATGACCTAG  
TTTTATATTTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCA  
AGAAACAAAAAGAAGCCAAAAGCAGAAGGCTCCAATATGAACAAGATAAATCTATCTTCAA  
GACATATTAGAAGTTGGGAAAATAATTCATGTGAAGTAGACAAGTGTGTTAAGAGTGATAAG  
TAAATGCACGTGGAGACAAGTGCATCCCCAGATCTCAGGGACCTCCCCCTGCCTGTCACCT  
GGGGAGTGAGAGGACAGGATAGTGCATGTTCTTTGTCTCTGAATTTTTAGTTATATGTGCTG  
TAATGTTGCTCTGAGGAAGCCCCTGGAAAGTCTATCCCAACATATCCACATCTTATATTCCA  
CAAATTAAGCTGTAGTATGTACCCTAAGACGCTGCTAATTGACTGCCACTTCGCAACTCAGG  
GGCGGCTGCATTTTAGTAATGGGTCAAATGATTCACTTTTTATGATGCTTCCAAAGGTGCCT  
TGGCTTCTCTTCCCAACTGACAAATGCCAAAGTTGAGAAAAATGATCATAATTTTAGCATAA  
ACAGAGCAGTCGGGGACACCGATTTTATAAATAAACTGAGCACCTTCTTTTTAAACAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 208**

MASLGQILFWSIISIIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI  
KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASRLKKNVQLTD  
AGTYKCYIIITSKGKGNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD  
QGANFSEVSNTSFELNSENVTMKVVSVLNVTINNTYSCMIENDIAKATGDIKVTSESEIKRR  
SHLQLLNSKASLCVSSFFAISWALLPLSPYMLK

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**FIGURE 209**

[illegible]



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**FIGURE 210**

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMPFL  
LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS  
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

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**FIGURE 211**

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG  
GAAGATGACAGCAATTATAGCAGGACCCTGCCAGGCTGTGCGAAAAGATTCCGCAATAAACT  
TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT  
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGCATCCTCG  
TTGCTGGTATCACTGCAGTGCTTGTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT  
TCATGGGAAAAATCCTGTGTCAACAGCATTGCCTCTGAATGTCCCTCACATGCCAACACCAG  
CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT  
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT  
GCTGAAGAACACTTTTCATTTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG  
CGATGCCCTGGACCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG  
AATCTAATGGAACCTCCTGTCGTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC  
TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTC  
CAACGTCAGTAACGCCACCTGTCAGTTCCTGTCTGGTGAAAACAAGACTCTTGGAGGAGTCA  
TCTTTCGAAAGTTTGAGTGTGCAAATGTAAACAGCTTAACCCCCACGTCTGCACCAACCACT  
TCCCACAACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG  
GGGACTGCTGCCCCTGAGGGTCCTGGGGCTGCACTTTGCCCAGCACCCCATTTCTGCTTCTCTG  
AGGTCCAGAGCACCCCCTGCGGTGCTGACACCCTCTTTCCTGCTCTGCCCCGTTTAACTGC  
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA  
AAGCACTGGTTCATTCACTGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 212**

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR  
LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE  
CPACYESNGTSCRGKPKWCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK  
TLGGVIFRKFEKANVNSLTPTSAPTTSNHNVGSKASLYLLALASLLLRGLLP

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**FIGURE 213**

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA  
GGGCTTGCCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCC**ATG**GTCCCCGCCGCCG  
GCGCGCTGCTGTGGGTCTGCTGCTGAATCTGGGTCCCCGGGCGGGGGGCCCCAAGGCCTG  
ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCATGACCCGCAG  
CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA  
ATGATGCCATGGCCGACGCCGACCGCTGGCTGGACCAGCGGCTGCCGAGCTCTTGGCCGCC  
ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA  
GGGGGTTGTGATTAATGCCGGAAGGATAGCACCAGCAGAGAGCTTCCAGTGCGACTCCCA  
ATACAGCGGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG  
ACTTCAAGCCTGCCGCGCTCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC  
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTCACCCTCACCCACAG  
CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC  
TGCAAGTCGGGCACCATGAGCCGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCT  
TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGACCTATCAACAATGTC  
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT  
GCCTCTCAGAGCACCACAGTACCAGGACCACCACTACCCCTTCCCCACCATCCACCTCAG  
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCTGCCAGCCCTGGCTTTTTGGAAACGGGTCA  
GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTACAGAGATGCAACCAATA  
GACAGAAACCAGAGG**TAA**TGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT  
CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTTAGTACAGAAAAACAAACTGGAAAA  
CACAA

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**FIGURE 214**

MVPAAGALLWVLLLNLGPRAAGAQGLTQTPTMQRVSLRFGGPMTRSYRSTARTGLPRKTRI  
ILEDENDAMADADRLAGPAAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL  
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP  
SPSPTAMPSPEDLRLVLPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC  
TYQQCPCNRLREECPLDTSLCDTNCASQSTTSTRTTTTTPTIHLRSSPSLPPASPCPALA  
FWKRVIRIGLEDIWNSLSSVFTEMQPIDRNQR

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**FIGURE 215**

CCCCGGTCCGACCCACGCGTCCGGGGAGAAAGGATGCCCGGCCCTGGCGGCGCGGTTGGTCCTGCTAGCTGGGGCA  
GCGGCGCTGGCGAGCGGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGACTGCGTACTGCAGTGCGAAGAGCA  
GAACTGCTCTGGGGGCGCTCTGAATCACTTCCGCTCCCGCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCT  
GTCGGGACGACTGTAAGTATGAGTGTATGTGGGTACCGTTGGGCTCTACCTCCAGGAAGGTACAAAGTGCCT  
CAGTTCATGGCAAGTGGCCCTTCTCCCGTTCTGTTCTTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTCT  
CAATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCCATGTACCACA  
CCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGTCTTCCACACCAGGGACACTGAC  
CTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCATCTACACTCAATCTACCTGTGCTGCGTCAGGAC  
CGTGGGGCTGCAGCACCCAGCTGTGGTCAGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGCACGTCT  
CCTACCTGAGCCTCATCCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTG  
GTGTGGTGGCTGGCCTGGTGCCTGTGGAACCAGCGGCGGCTGCCTCACGTGCGCAAGTGCCTGGTGGTGGTCTT  
GCTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCACCGCTCTTCTGGGTCTGGATGCCCATGCCA  
TCTGGCACATCAGCACCATCCCTGTCCACGTCCTCTTTTTCAGCTTTCTGGAAGATGACAGCCTGTACCTGCTG  
AAGGAATCAGAGGACAAGTTCAAGCTGGACTGAAGACCTTGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCC  
GCCCTGCTGGCCTCCCTTCTCCCTCAACCCTTGAGATGATTTTCTCTTTTCAACTCTTGAAGTGGACATGA  
AGGATGTGGGCCCAGAATCATGTGGCCAGCCCACCCCTGTGGCCCTCACCAGCCTTGGAGTCTGTTCTAGGG  
AAGGCCTCCAGCATCTGGGACTCGAGAGTGGGAGCCCTCTACCTCCTGGAGCTGAAGTGGGGTGGAACTGA  
GTGTGTTCTTAGCTCTACCGGGAGGACAGCTGCCTGTTCTCCTCCCCACCAGCCTCCTCCCCACATCCCCAGCTG  
CCTGGCTGGGTCTGAAGCCCTCTGTCTACCTGGGAGACCAGGGACCACAGGCCCTAGGGATACAGGGGGTCCC  
CTTCTGTTACCAACCCCCACCCTCCTCCAGGACCACTAGGTGGTGCTGGATGCTTGTCTTTGGCCAGCCAA  
GGTTCACGCGATTCTCCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTCAACCTGACC  
GTTGCCCTAGCCAGGTTCCCAGGAGGCCTCACCATACTCCCTTTTCAGGGCCAGGGCTCCAGCAAGCCCCAGGGCA  
AGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTGCGGAGTGTGGGCCAGGCTGAGTGCATAGG  
TGACAGGGCCGTGAGCATGGGCCTGGGTGTGTGTGAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGT  
CGGGGAAGAGGTGTGGCTTCAAAGTGTGTGTGTGAGGGGGTGGGTGTGTAGCGTGGGTAGGGGAACGTGTG  
TGCGCGTGTGGTGGGCATGTGAGATGAGTGACTGCCGTTGAATGTGTCCACAGTTGAGAGGTTGGAGCAGGAT  
GAGGGAATCCTGTACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCAAGACGCCACCTGGGCGGACAGC  
CAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGGTGGCCCTTTGCCCGCTCCTGCAAC  
CTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAGCAGCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGC  
TGGGGCTCTCTCCATCCTCCTTTCTCCTTGCCTTCGCATGGCTGGCCTTCCCTCCAAAACCTCCATTCCCCT  
GCTGCCAGCCCCCTTTGCCATAGCCTGATTTTGGGGAGGAGGAAGGGGCGATTGAGGGAGAAGGGGAGAAAGCT  
TATGGCTGGGTCTGGTTTCTTCCCTTCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGGCAGGCAGGGGCC  
ACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGCCCTGGCATGTTCTGCCCCACAGG  
AATAGAATGGAGGGAGCTCCAGAACTTTCCATCCCAAAGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTGT  
CTCTGCCCTGACCCCTTGTCCCTCTTTGAGGGAGGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTG  
GCCTGCGCTAGCTTCTTTTGATACTGAAACTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAA  
TTCCAAGCCTCAAAAAAAAAAAAAAAAAA

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**FIGURE 216**

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW  
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSSRFLFFQEPASAVASFLNGLASLVMLCR  
YRTFVPASSPMYHTCVAFAWVSLNAFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR  
TVGLQHPAVVSAFRALLLMLTVHVSYSLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR  
RLPHVRKCVVVVLLQLGLSLELLDFPPLFWVLDAHAIWHISTIPVHVLFFSFLEDDSLYLL  
KESEDKFKLD

**Important features:****Signal peptide:**

amino acids 1-20

**Transmembrane domains:**

amino acids 105-123, 138-156, 169-185, 193-209, 221-240, 256-272

**N-glycosylation site.**

amino acids 40-44

**N-myristoylation site.**

amino acids 43-49

**CUB domain proteins profile.**

amino acids 285-302

**Amiloride-sensitive sodium channels proteins.**

amino acids 162-186

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**FIGURE 217**

[illegible]



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**FIGURE 218**

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL  
DAEVLEVFPHTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLK GKRLDINTN  
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV  
RLINKFNSSSSSLEEKIAALFDLEYVHQM DNAQDLLSFGGLQVVINGLNSTEPLVKEYAAF  
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL  
GGLQVLR TLVQEKGTEVLAVRVV TLLYDLVTEKMFAEEEAELTQEMSPEKLQQYRQVHLLPG  
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS  
LELQDGEDEGYFQELLGSVNSLLKELR

**Important features:****Signal peptide:**

amino acids 1-29

**Hypothetical YJL126w/YLR351c/yhcX family protein.**

amino acids 364-373

**N-glycosylation site.**

amino acids 193-197, 236-240

**N-myristoylation site.**

amino acids 15-21, 19-25, 234-240, 251-257, 402-408, 451-457

**Homologous region SLS1 protein.**

amino acids 68-340

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**FIGURE 219**

[illegible]

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**FIGURE 220**

MGAAVFFGCTFVAFGPAFALEFLITVAGDPLRVIIILVAGAFFWLVSLLLASVVWFILVHVTDR  
SDARLQYGLLI FGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS  
FGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAAIILLHTFWGVVFFDACERRR  
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLLCKD

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**FIGURE 221**

AAGCTGGTTTAAGGAAGCAGAGGAGGGTTAGATTCGTTGAGTGAGGACGGAAGATCAACCCA  
TTTCCATTCCGCCAGATGGCCTATGTTTCTGGTCTCTCCCTTCGGNATCATCAGTGGTGTNT  
TNTCTGTTATCAATATTTTGGCTGATGCANTTGGGCCAGGTGTGGTTGGGATCCATGGAGAC  
TCACCCTATTANTTCCTGANTTCAGCCTTTNTGACAGCAGCCATTATCCTGCTC

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**FIGURE 222**

GACCGACCGTTCAGATGCCCCGGTTCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG  
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG  
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN  
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTTGGNTGATGCAN  
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCTATTAATTCCTGAATTCAGCCTTT  
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTGTTTTTTGATGCCTGTGA  
GAGGAG

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**FIGURE 223**

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCGGTTTCCCCCTTCCCTTTCCCCG  
GGGTCTGGGGTGACATTGCACGGGCCCCCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCC  
CCAGNTGGNGCGCCCTTCCCATTTCCTGTCTGGTCAGGCCCCACCCCTTCCCACNTG  
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTCGCGTTCGGCCCGGCCTTCG  
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA  
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGAC  
CGACCGGTCAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTCC  
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA  
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG  
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTTG  
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

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**FIGURE 224**

GTAAAAGAAAGTGGCCGGACCTTCATTGGGGTTTCGGTTCCCCCCTTCCCNNTCCCCGGGG  
TCTGGGGGTGACATTGCACCGCGCCNCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCCC  
CAGNTGGCGCGCCCCTCCCATTTGCCTGTCCCTGGTCAGGCCCCACCCCCCTTCCCACCTGA  
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTCGCGTTCGGGCCCCGGCCTTC  
GCGCTTTTCTTGATCACTGTGGCTGGGGACCGCTTCGCGTTATCATCCTGGTCGCAGGGGC  
ATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGA  
CCGACCGGTCAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTC  
CTTCTACAGGAGGTGTTCCGCTTTCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT  
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG  
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTT  
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

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**FIGURE 225**

GCCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCGGTGCCAGAGCCCAGGAGGAGGCAG  
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCACCCCC  
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAGGAGAGG  
TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCTCCTTGCCCTGTCTGGAGGCTGCT  
AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCGCAGTGCCGATGGTGCCCCGT  
CCTTGTGGTTTCCTCTCTACCTGGGGAAATAAGGTGCAGCGGCCATGGCTACAGCAAGACCCC  
CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTACAGAGCATGTT  
CTCGCCAACAATGATGTTTCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA  
GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCCGGTGGGATGACAGCAGCAGCCGCATCATCA  
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC  
CAGCTCTACTGCGGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCACTGCAG  
GAAGAAAGTTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC  
AGCAGATGTTCCAGGGGGTCAAATCCATCCCCACCCTGGCTACTCCCACCCTGGCCACTCT  
AACGACCTCATGCTCATCAAAGTGAACAGAAGAATTCGTCCCCTAAAGATGTCAGACCCAT  
CAACGTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGACAA  
CCAAGAGCCCCCAAGTGCACCTCCCTAAGGTCCCTCCAGTGCTTGAATATCAGCGTGCTAAGT  
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA  
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCC  
TGCAGGGACTCGTGTCCTGGGGAGATTACCCTTGTCGCCGGCCCAACAGACCGGGTGTCTAC  
ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTTGAGTCAT  
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTTCAG  
ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTTCATCTCTCCAGCCCCTGACCCCATGTCT  
CCTGGACTCAGGGTCTGCTTCCCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCTGG  
GAACAATTTCCAAAAGTGTCCAGGGCGGGGGTTGCGTCTCAATCTCCCTGGGGCACTTTTCAT  
CCTCAAGCTCAGGGCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA  
CTGAGAAGTGGAATAAAAAA



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**FIGURE 226**

MATARPPWMWVLCALITALLGVTEHVLANNNDVSCDHPSNTVPSGSNQDLGAGAGEDARSDD  
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS  
PVYESGQQMFQGVKSIPHPGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCP SAGTKCL  
VSGWGTTKSPQVHF PKVLQCLNISVLSQKRCE DAYPRQIDDTMFCAGDKAGRDSCQGD SGGP  
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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**FIGURE 227**

**ATGGTCAACGACCGGTGGAAGACCATGGGCGGGCGCTGCCCAACTTGAGGACCGGGCCGCGCGA**  
CAAGCCCGCAGCGGCCGAGCTGCGGCTACGTGCTGTGCACCGTGCTGCTGGCCCTGGCTGTGC  
TGCTGGCTGTAGCTGTACCGGTGCCGTGCTCTTCTGAACCACGCCCACGCGCCGGGCACG  
GCGCCCCACCTGTCTCAGCACTGGGGCTGCCAGCGCCAACAGCGCCCTGGTCACTGTGGA  
AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCCGACCTCACCGACA  
GCTTCGCACGCCTGGAGAGCGCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC  
CAGCCACGGCTGGTGGGCGACCAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC  
CCGGCTGCTGGCCCGAGCCTCAGAGCTGCAGACGGAGTGCATGGGGCTGCGGAAGGGGCATG  
GCACGCTGGGCCAGGGCCTCAGCGCCCTGCAGAGTGAGCAGGGCCGCTCATCCAGCTTCTC  
TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACCTCCGTACGCGACATCCTGGATGCCCT  
GCAGAGGGACCGGGGGCTGGGCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCC  
GGGGAACCCGGCCCCGGGGCTGTGCCACTGGCTCCCGGCCCGAGACTGTCTGGACGTCTCT  
CTAAGCGGACAGCAGGACGATGGCGTCTACTCTGTCTTTCCACCCACTACCCGGCCGGCTT  
CCAGGTGTACTGTGACATGCGCACGGACGGCGGGCTGGACGGTGTTCAGCGCCGGGAGG  
ACGGCTCCGTGAACCTTCTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC  
GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT  
GCACGTGGACCTGGAGGACTTTGAGAATGGCAGGCCTATGCCCGCTACGGGAGCTTCGGCG  
TGGGCTTGTTCTCCGTGGACCCTGAGGAAGACGGGTACCCGCTCACCCTGGCTGACTATTCC  
GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGGCATGAGGTTACACCACCAAGGACCGTGA  
CAGCGACCATTCAGAGAACAACCTGTGCCGCTTCTACCGCGGTGCCTGGTGGTACCGCAACT  
GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCCTCCTATGCCGACGGC  
GTGGAGTGGCTCCTCCTGGACCGGCTGGCAGTACTCACTCAAGTTCTCTGAGATGAAGATCCG  
GCCGCTCCGGGAGGACCGCTAGACTGGTGACCTTGTCCTTGCCCTGCTGGTCCCTGTCTCGC  
CCCATCCCCGACCCACCTCACTCTTTCGTGAATGTTCTCCACCCACCTGTGCCTGGCGGAC  
CCACTCTCCAGTAGGGAGGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT  
CACACATCGCCTTCTCGCCGTCCCCACCCCTCCATTGAGCAGCTCACTGATCTCTTGCTC  
TGCTGATGGGGGTGGCAAACTTGACGACCCCAACTCCTGCCTGCCCCCACTGTGACTCCGG  
TGCTGTTTGCCGTCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCTCTGCCCTGCC  
GGCCAAATACCCGGCATTATGGGGACAGAGAGCAGGGGGCAGACAGCACCCCTGGAGTCCTC  
CTAGCAGATCGTGGGGAATGTCAGGTCTCTCTGAGGTGAGGTCTGAGGCCAGTATCCTCCAG  
CCCTCCCAATGCCAACCCCAACCCGTTTCCCTGGTGCCAGAGAACCCACCTCTCCCCAA  
GGGCCTCAGCCTGGCTGTGGGTGGGTGGCCCCATCCTACCAGGCCCTGAGGTGAGGATGGG  
GAGCTGCTGCCTTTGGGGACCCACGCTCCAAGGCTGAGACCAGTTCCCTGGAGGGCCACCCAC  
CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCTCTTACCTGCTGTGCCACCTGCTCTCTG  
TCTCAAATGAGGCCCCAACCCATCCCCACCCAGCTCCCGGCCGTCTCTACCTGGGGCAGC  
CGGGGTGCCATCCCATTTCTCCTGCCTCTGGAAGGTGGGTGGGGCCCTGCACCGTGGGGCT  
GGACTGCGCTAATGGGAAGCTCTTGTTTTCTGGGCTGGGGCTAGGCAGGGCTGGGATGAG  
GCTTGTAACCCCCACCACCAATTTCCAGGGACTCCAGGGTCTGAGGCCTCCCAGGAGG  
GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCTTGCC  
ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCGGCCGAGTGCTCAAGGGACAGGGA  
CCACCTCACCAGGGCAAATGGGGTCGGGGGACTGGGGCACCAGACCAGGCACCACTGGACA  
CTTTCTTGTTGAATCCTCCCAACACCCAGCAGCTGTCTATCCCCACTCCTTGCTGTGCACACA  
TGCAGAGGTGAGACCCGACAGGCTCCCAGGACCAGCAGCCACAAGGGCAGGGCTGGAGCCGGG  
TCCTCAGCTGTCTGCTCAGCAGCCCTGGACCCGCGTGCCTTACGTGAGGCCAGATGCAGGG  
CGGCTTTTCCAAGGCCTCCTGATGGGGGCTCCGAAAGGGCTGGAGTCAGCCTTGGGGAGCT  
GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGAGGTGGCTTCCCTCCAAAGGACACCCGATGGCA  
GGTGCCTAGGGGGTGTGGGGTTCCGTTCTCCCTTCCCTCCCACTGAAGTTTGTGCTTAAAA  
AACAAATAAATTTGACTTGGCACCCTGGGGGTGGTGGGAGAGGCGGTGTGACCTGGCTCTC  
TGTCCCAGTGCCACCAGGTATCCACATGCGCAG

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**FIGURE 228**

MVNDRWKTMGGAAQLEDPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT  
APPPVVSTGAASANSALVTVRADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA  
QPRLVGDQEQELLDTLADQLPRLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL  
SESQGHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL  
LSGQQDDGVYSVFPHTYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT  
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAAYARYGSFGVGLFSVDPEEDGYPLTVADYS  
GTAGDSLLKHSGMRFTTKDRSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASADG  
VEWSSWTGWQYSLKFSEMKIRPVREDR

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**FIGURE 229**

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT  
TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCAGGGCAATCCGACCACATTTCACTCT  
CACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG  
ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTCGGCATCCAGAGCCC  
CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC  
TTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTACTACC  
AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATACGTCC  
CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC  
TGAAAACTCTGTCTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG  
AACAATGGAAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG  
GACTGTAAATATTTCTGCCTTAGTGAAAACTCTACCATGCTGAAGATAAACAAACAAGAAGA  
CCTGGAATTTGCCGCTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT  
TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGATGGAACCCCTTTCATTCTGAACTG  
TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG  
GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA  
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCGAAGGTGACTTGAATTCGCC  
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT  
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG  
TTTCCTGTTTCAAGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA  
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCCATAATGTCATCTGCCTTCTTG  
GCTTAGAGATAACTTTTAGCTCTCTTTCTTCTCAATGTCTAATATCACCTCCCTGTTTTCAT  
GTCTTCCTTACACTTGGTGGAATAAGAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC  
ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC  
AGCAAATACACAAGGAATTCTTTTTGTTTGTTCAGTTCATACTAGTCCCTTCCCAATCCAT  
CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG  
AATCTCAAATCTCAATGCCTTATAAGCATTCCCTTCCCTGTGTCCATTAAAGACTCTGATAATTG  
TCTCCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCTCTCCGTTTCATATCAG  
AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAGTGAGCCTCTTCA  
TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTCAG  
GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

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**FIGURE 230**

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSSTWRPVALTLLTLCLVLL  
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE  
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS  
QSYSEFFYSYWTGLLRPD SGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD  
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

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**FIGURE 231**

AATTTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG  
ATGATGATGGGACACCACCATGAGCCTGCATTNTCAAGCTTTTGCCACAATTCGGCATCCAG  
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTTTCAACGTGGCGACCAGTGGCCCTGACCCTG  
CTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTA  
CTACCAGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATA  
CGTCCCAAGAGTTGCAATTTNTTCAAGTCCAGAATATAAAGCTTGCAGGAAGNTGCAGCAT  
GTGGCTGAAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGGAACTTTGAAGGAGGGCAA  
AGTNTCCTCATNTACTATACACACCACTTCCC

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**FIGURE 232**

·GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGGCGCGGCTC  
CGGGGATTTCGGCTCGGGCCGCTGGCTCTGCTCTGCGGGGAGGGAGCGGGCCCCGCGGGG  
CCCGAGCCCTCCGGATCCGCCCCCTCCCCGGTCCCGCCCCCTCGGAGACTCCTCTGGCTGCT  
CTGGGGGTTCCGCCGGGGCCGGGGACCCGCGGTCCGGGCGCC**ATG**CGGGGCATCGCTGCTGCTG  
TCGGTGCTGCGGGCCGAGGGCCCGTGGCCGTGGGCATCTCCCTGGGCTTACCCTGAGCCT  
GCTCAGCGTACCTGGGTGGAGGAGCGTGCGGCCAGGCCCGCCCCAACCTGGAGACTCTG  
AGCTGCCGCCGCGCGGCAACACCAACGCGGCGCGCGGCCCAACTCGGTGCAGCCCCGAGCG  
GAGCGCGAGAAGCCCCGGGGCCGGCGAAGGCGCCGGGGAGAATTGGGAGCCGCGCGTCTTGCC  
CTACCACCCTGCACAGCCCGGCCAGGCCGCCAAAAAGGCCGTGAGGACCCGCTACATCAGCA  
CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC  
ACGCTGGGCGTGGCCGTGAACCGCACGCTGGGGCACCGGTGGAGCGTGTGGTGTCTGAC  
GGGCGCACGGGGCCGCCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC  
CCATTGGACACCTGCACCTGGCGCTGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC  
TGGTTCTTCCTGGTGCCTGACACCACCTACACGAGGCGCACGGCCTGGCACGCTTAACCTGG  
CCACCTCAGCCTGGCCTCCGCCGCCACCTGTACCTGGGCCGGCCCCAGGACTTCATCGGCG  
GAGAGCCACCCCCGGCCGCTACTGCCACGGAGGCTTTGGGGTGCTGCTGTGCGCATGCTG  
CTGCAACAACCTGCGCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGCGCGCCCTGA  
CGAGTGGCTGGGTGCTGCTGATTCTCGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG  
GGGTGCACTATAGCCATCTGGAGCTGAGCCCCGGGGAGCCAGTGACAGGAGGGGGACCCTCAT  
TTCCGAAGTGCCCTGACAGCCCACCCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA  
AGCTTTCGCCCGAGCTGAACCTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA  
TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGCCCGTGGGTATT  
CCAGCACCATCCCGCCCGGCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA  
GCACGCTTTCTCTGCGCCGATGGCTCACCCCGCTGCCCACTGCGTGGGGCTGACCGGGCTG  
ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCCGGCCTTG  
CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCGGGGTATGGA  
ATACACGCTGGACTTGACAGCTGGAGGCACTGACCCCCAGGGAGGCCGCCGGCCCCCTCACTC  
GCCGAGTGACGCTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCTGTGCCCTATGTCACT  
GAGCCCTCAGCTCACTGTGCTGCTGCCTCTAGCTGCGGCTGAGCGTGACCTGACCCCTGG  
CTTCTTGAGGGCCTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC  
TGCTGCTACTGTATGAGCCGCGCCAGGCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT  
GTCAAGGCCCACGTGGCAGAGCTGGAGCGGCGTTTCCCCGGTGCCCGGGTGCCATGGCTCAG  
TGTGCAGACAGCCGCACCCTCACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC  
TGGACACACTGTTCTCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCTGAACCGC  
TGCCGCATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA  
CCCAGGTGTGGCCCCACCACAAGGGCCTGGGCCCCAGAGCTGGGCCGTGACACTGGCCGCT  
TTGATCGCCAGGCAGCCAGCGAGGCCTGCTTCTACAACTCCGACTACGTGGCAGCCCCGTGGG  
CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGAGCTGCTGGAGAGCCTGGATGTGTACGAGCT  
GTTCTTCCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGGCGCTGCTGCAGCGCT  
ACCGGGCCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCTCCAGAGC  
GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG  
CAACAGCACCT**TGA**CCCCACCCTGTCCCCGTGGGCCGTGGCATGGCCACACCCACCCCACTT  
CTCCCCAAAACCAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC  
AAGCTGGCCCACTGGTCCCCTCTCTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG  
GGAGTGCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT  
GCTGATTGCGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACCCAGCCCTGC  
CTCTGGGCCCTGGGGGCTGGGCTGTAGAAGAGTTGTTGGGGGAAGGAGGGAGCTGAGGAGGGG  
GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA  
AGTGTGGAAAAA

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**FIGURE 233**

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP  
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAACKAVRTRYISTELGIRQRLVAVL  
TSQTTLPTLGAVVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEERPIGHLHLALRHLE  
QHGDDEFDWFFLVPDDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG  
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCIL DATGVGCTGDHEGVHYSHLELSPGEP  
VQEGDPHFERSALT AHPVRDPVHMYQLHKAFARAE LERTYQEIQELQWEIQNTSHLAVDGDRA  
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTALEELN  
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI  
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA  
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPRLMDLLSKKHPLDTLFLLAGPDTVL  
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQGPPELGRDTGRFDRQAASEACFYNS  
DYVAARGRLAAASEQEEELLES LDVYELFLHFSSLHVLR AVEPALLQRYRAQTCSARLSEDL  
YHRCLQSVLEGLGSRTQLAMLLFEQE QGNST



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**FIGURE 234**

GCTCTGGCCGGCCCCGGCGATTGGTCAACGCCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT  
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT  
AGCTATTAGCCAATTTCGGCAGGGCCCCGCTTTTTAGAAAGCTTGATTTCCCTTTGAAGATGAAAG  
ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA  
CTGTATCCACCCAAATGTCACCGATTTCTTCCTATGCAGGAAATGAGCAGACCCATCAATAA  
GAAATTTCTCAGCCTGGCCGAAAATGGTTGGCCCCACGAAGCCACGACAACCTGGAGGCAAAG  
AGGGTTGCTCAACGCCCCGCCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG  
GCGGAGGCGGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT  
TTCCCCGCCCCTGAGACCCTGCAGACCATCTGTC**ATGG**CGGCTGGGCTGTTTGGTTTGAGC  
GCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGCTCCCGGCCGCCCGCGTCCGCTGGGA  
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC  
CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACCTTGATGAGAAGAACCCA  
GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT  
CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA  
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC  
CTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAG**TC**  
**A**CCAGTTGCTAAGTGGGGCTCAAGAAGCACCGCCTTCCCCACCCCCTGCCTGCCATTCTGAC  
CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

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**FIGURE 235**

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE  
DENLYEKNPD SHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER  
LVKYREANGLPIMESNCFDPSKIQLPEDE

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**FIGURE 236**

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGC  
TCCCGGCCGCCCCGCTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT  
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA  
CGAAAACCTGTATGAGAAGAACCCAGACTCCCATGGTTATGACAAGGACCCCGTTTTGGACG  
TCTGGAACATGCGACTTGTCTTCTTCTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC  
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT  
TGTGAAATACCGAGAGGCCAATGGCCTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCA  
AGATCCAG

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**FIGURE 237**

GCGGCGGCTATGCCGCTTGCTCTGCTCGTCCTGTTGCTCCTGGGGCCCCGGCGGCTGGTGCCT  
TGCAGAACCCCCACGCGACAGCCTGCGGGAGGAACTTGTCATCACCCCGCTGCCTTCCGGGG  
ACGTAGCCGCCACATTCCAGTTCCGCACGCGCTGGGATTTCGGAGCTTCAGCGGGAAGGAGTG  
TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA  
GCTGCACCTGTCATTACACAAGGCTTTTGGAGGACCCGATACTGGGGGCCACCCTTCCTGC  
AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA  
TCTTGGAAGGAGCTCAGTAATGTCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA  
CTCCACCAACACAGTCACTCCCCTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG  
ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC  
CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA  
TCGCTTGTTCCACACCAGCTACCACTCCCAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG  
CAGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC  
ATCACGGGGCAGGGAAGAAAGACTGGTCCCTCTTCCGGATGTTCTCCCGAACCCCTCACGGA  
GCCCTGCCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACTACAACCAGGACA  
ACGAGACATTAGAGGTGCACCCACCCCGACCACTACATATCAGGACGTCACTCTAGGCACT  
CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACCTCTCGAAACCT  
CAACATCCAGCTCAAGTGGAAGAGACCCCGAGAGAATGAGGCCCGCCAGTGCCCTTCCTGC  
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC  
AACACCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG  
GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAACCAAGTTACATCC  
ACTACCAGCCTGCCAGGACCGGCTGCAACCCACCTCCTGGAGATGCTGATTAGCTGCCG  
GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA  
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCTCAGCGCCCTTGTGCCCCA  
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCCTCTTCAACAGCCTGTTCCCA  
GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC  
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT  
GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT  
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCGCCCGAGGTGTCCCCCACTCTGATT  
CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT  
TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTCAGGGC  
CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTGGAATTTGAATTAA  
CTTAGAAATTCATTTCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA  
AGTGGTCGGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACACAGAAAGGTC  
GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGGA  
TGGAGTTTACTGTTTGTGGAATAAAAACGGCTGTTTCCGTGGAAAAA

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**FIGURE 238**

MPLALLVLLLLGPGGWCLAEP PRDSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY  
RLFPKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVTDVDSWK  
ELSNVLSGIFCASLNFIDSTNTVTPTASF KPLGLANDTDHYFLRYAVLPREVVCTENLTPWK  
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCRNARCTSSISWELRQTLSVVFDAFITG  
QGKKDWSLFRMF SRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT  
YAIYDLLDTAMINNSRNLNIQLKWKRP PENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH  
PYRAFPVLLLDTPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDR LQPHLLEMLIQLPANS  
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAK PVDWEESPLFNSLFPVSD  
GSNYFVRLYTEPLL VNLPTPDFSMPYNVICLTCTVVAVCYGSFYNLLTRTFHIEEPRTGGLA  
KRLANLIRRARGVPPL

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**FIGURE 239**

CAACATGGGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTTGTGACCCTGGTGG  
CTGTGGAAGGAGTTAAAGAGGGTATAGAGAAAGCAGGGGTTTGCCCAGCTGACAACGTACGC  
TGCTTCAAGTCCGATCCTCCCCAGTGTACACAGACCAGGACTGTCTGGGGGAAAGGAAGTG  
TTGTTACCTGCACTGTGGCTTCAAGTGTGTGATTCTGTGAAGGAACTGGAAGAAGGAGGAA  
ACAAGGATGAAGATGTGTCAAGGCCATACCTTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC  
TCCTCCTCTACCAGGTGTCCTCAGAAATTGATGCTGGGTCCTTTCTACCTCTGGGGGTCACTC  
TCACTTGGCACCTGCCCCTGAGGGTCCTGAGACTTGGAATATGGAAGAAGCAATACCCAACC  
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTTCCCCAAAAAGAGGGAAGAGTCACAAAAAG  
TCCAGACCCAGGGACGGTACTTTCCCTCTCTACCTGGTGCTCCTCCCTAATGCTCATGAAT  
GGACCCCTCATGAATGAAACCAGTGCCCTTATAAGAGACCCCAAAGAGCTGCCTTGCCCTTC  
TGCAATGTGTGATCACAGCTAGAAGGCACTGTCAGAGAAGAGAACTGGTCCTCACCAGATG  
CTGAATCTGCTGGTGCCTTGATCTTGGACTTCCCAGCCTCTAGAAGTGTAAAGAAATAAATAT  
TTGCTGTTTATAATCCAA

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**FIGURE 240**

MGSSSFVLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC  
YLHCGFKCVIPVKELEEKGKDEDVSRPYPEPGWEAKCPGSSSTRCPQK

**Signal sequence:**

amino acids 1-19

**N-myristoylation sites:**

amino acids 23-29, 27-33, 32-38, 102-108

**WAP-type 'four-disulfide core' domain signature:**

amino acids 49-63

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**FIGURE 241**

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG  
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC  
TCTAGAACCCGACCCACCACCATGAGGTCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG  
CGTCCAGTGGTCCCTTGCTTCTGGCTGTCCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTA  
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATTAAAGAAAGGTCT  
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA  
TGCAGAGCCAGCGCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCCAAGGGCCACACCA  
CCGGAGACAGAGGAAAGGAGGCCAACCAGGCACCGCCGGAGGAGCAGGACAAGGTGCCCCAC  
ACAGCACAGAGGGCAGCATGGAAGAGCCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC  
ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC  
AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG  
GTGTCAGAGAAGCACCAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCCAAAGTCA  
GCACAGAATGCTGGCTCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA  
CAGCAGTCATCCACCTAAGGAGAAGAAACCTCAGGCCACCCACCCCTGCCCTTTCCAG  
AGCCCCACGACGCAGAGAAACCAAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG  
GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG  
TGAAGATCAAAGCCTCCAAGTCGCTGTGGCTCCAGAACTCTTTCTGCCCCAACCTCACTCTC  
TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC  
CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAAGGTCGTGACACGCTTCCCTCCAG  
TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT  
GCCGTGGTGGGCAACGGGGGCATCCTGAACAACTCCCACATGGGGCCAGGAGATAGACAGTCA  
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAGGCTACGAACAGGATGTGGGGACTC  
GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT  
CGGGGTTTCAAGAACGTGCCTCTTGGAAGGACGTCCGCTACTTGCACTTCTTGGAAGGCAC  
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT  
TCTGGTTCAGGCACAGACCCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG  
TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCCTGGA  
TGGTGGCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTT  
AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT  
CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA  
GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC  
CCGGAAGTGCACAAAGCCAAGAAGTGAACCGGGGCCAGGGCTGCCATGGTCTCCTTGCTGCTC  
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA  
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT  
GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCTGAGGCCAGG  
GATTTTTTAATTAAATGGGGTGATGGGTGGCCAATACCACAATTCCTGCTGAAAAACACTCTT  
CCAGTCCAAAAGCTTCTTGATACAGAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG  
GTTTGAATTCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC  
AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG  
TCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAAGTGAATAATAACAAATGATTGTT  
GTCCATGGAAAGGCAAATAAATTTTCTACAGTGAAAAA



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**FIGURE 242**

MRSC LWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP  
KSQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW  
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNNGGQTRKLTASRTVSEKHQG  
KAATTAKTLIPKSQHRMLAPTGA VSTRTRQKGVTTAVIPPEKKPQATPPPAPFQSPTTQRN  
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLELPNLTFLFLDSRHF  
NQSEWDRLEHFAPPPFGFMELNYSLVQKVVTFRPPVPQQQLLLASLPAGSLRCITCAVVGNGG  
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGF TAFSLTQSLILGNRGFKNVP  
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEA FREALHMDRYLLHPDFL  
RYMKNRFLRSKTL DGAHWRIYRPTTGALLLLLTALQLCDQVSAYGFITEGHERFSDHYDTSW  
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRP GPGTAKAKN

**Cytoplasmic Domain:**

amino acids 1-10

**Type II Transmembrane Domain:**

amino acids 11-35

**Lumenal catalytic Domain:**

amino acids 36-600

**Ribonucleotide Reductase small subunit Signature:**

amino acids 481-496

**N-glycosylation Sites:**

amino acids 300-303, 311-314, 331-334, 375-378, 460-463

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**FIGURE 243**

CG**ATG**CGCGGACCCGGGCACCCCCTCCTCCTGGGGCTGCTGCTGGTGCTGGGGCCTTCGCCG  
GAGCAGCGAGTGGAAATTGTTCCCTCGAGATCTGAGGATGAAGGACAAGTTTCTAAAACACCT  
TACAGGCCCTCTTTATTTTAGTCCAAAGTGCAGCAAACACTTCCATAGACTTTATCACAACA  
CCAGAGACTGCACCATTCCTGCATACTATAAAAGATGCGCCAGGCTTCTTACCCGGCTGGCT  
GTCAGTCCAGTGTGCATGGAGGATAAG**TGA**GCAGACCGTACAGGAGCAGCACACCAGGAGCC  
ATGAGAAGTGCCTTGGAACCAACAGGGAAACAGAACTATCTTTATACACATCCCCTCATGG  
ACAAGAGATTTATTTTGCAGACAGACTCTTCCATAAGTCCTTTGAGTTTTGTATGTTGTTG  
ACAGTTTGCAGATATATATTCGATAAATCAGTGTACTTGACAGTGTTATCTGTCACTTATTT

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**FIGURE 244**

MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFRLYHNT  
RDCTIPAYYKRCARLLTRLAVSPVCMEDK

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**FIGURE 245**

GGGCTGGGCCCCGCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG  
CCCGACCCCGGCGCGCCAGCCCCACCATGCCACCCGCGGGGCTCCGCCGGGCGCGCCG  
CTCACCGCAATCGCTCTGTTGGTGCTGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT  
GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT  
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG  
CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT  
CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTCTGTTCTGTTGCTACCTGT  
ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC  
CCAGTGACAGCCAGTATACCCATACCCCCAGGACCCCCAAAGCTGGCCCTGCACCCCCACAGCC  
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC  
CAGTCTACAACCCTGCAGCTCCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC  
TGAGGAACCAGCCATGTCTCTGCTGCCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT  
CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA  
GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA  
ACTATGAGGGGTGGGGGGAGGGCTTGAATTATGGGCTATTTTACTGGGGGCAAGGGAGG  
GAGATGACAGCCTGGGTACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG  
CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGTGGGGGGAGGGAGGAGGT  
TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG  
CTAGATTAAAGCTGTAAAGACAAAA

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**FIGURE 246**

MPPAGLRRAAPLTAIALLLVLGAPLVLAGEDCLWYLDNRNGSWHPGFNCEFFTFCGTCYHRYC  
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLLSCCYLYRRRQQQLQSP  
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPPP  
YMPPQPSYPGA

**Transmembrane Domains:**

amino acids 10-28, 85-110

**N-glycosylation Site:**

amino acids 38-41

**N-myristoylation Sites:**

amino acids 5-10, 88-93

**FIGURE 247**

[illegible]

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**FIGURE 248**

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH  
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE  
HPPQEQIALLAPEPLLVLGYPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA  
ARMAFPCFDEPAFKASFSEIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA  
FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLFEFYEDYFSIPYPLPKQDLAA  
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL  
WLNEGFAKFMEFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD  
DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG  
FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD  
TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL  
TGLLKGTHTAVSSNDRASLINNAFQLVLSIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP  
MYKLMEKRD MNVETQFKAFILRLRLDLIDKQTTWDEGSVSEQMLRSELLLLACVHNYQPCV  
QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSTEKSQIEFALC  
RTQNKEKLQWLLDESFKGDKIKTQEFQILTILGRNPVGYPLAWQFLRKNWNKLVQKFELGS  
SSIAHVMVGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQTIIETIEENIGWMDKNFDKIR  
VWLQSEKLERM

**Signal peptide:**

amino acids 1-34

**N-glycosylation sites:**

amino acids 70-74, 154-158, 414-418, 760-764, 901-905

**Neutral zinc metallopeptidases, zinc-binding region signature:**

amino acids 350-360

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**FIGURE 249**

CAGCCACAGACGGGTCATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCCAC  
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC  
GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA  
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG  
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC  
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCCTGCT  
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCAGTCTGCTTGTCTATGG  
AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT  
GGCCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC  
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCCGTGGGTATGACTGAGA  
ACTGCAATAGGAAAGATTTTCTGACCTGTCATCGGGGGACCACCATTATGACACACGGAAAC  
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT  
GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG  
GCTGCAGCACTGTTGGGGCTCAAATTTCCAGAAGACCACCATCCACTCAGCCCCCTCCTGGG  
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG  
CAGCGTTCTGCTGAACCTCCCTCCCTCCTCAAGCTGCCCCCTGTCCCAGGAGACCGGCAGTGTC  
CTACCTGTGTGCAGCCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG  
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAT  
GAGCATTGAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTTGAACCACACCAGACAAATCG  
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT  
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG  
GTGGGGAGTGGTTTGCCCTTCCTGCTTAACTCTATTACCCCCACGATTCTTCACCGCTGCTGA  
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTTC  
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTATCTACTCACCTAACAGCA  
ACACTGGGGAGAGCCTGGAGCATCCGGAAGTGGCCTATGGGAGAGGGGACGCTGGAGGAGTG  
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA



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**FIGURE 250**

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTSCDSGLGCQDTLMLI  
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDEFNNLVNSLPLWAPQP  
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTTCYDGLLRRLRGGGIFSNLRVQGCMPPQPGCN  
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSENTEMCEVGQVCQETL  
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSSVLLN  
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLSGGGLSTKMSIQGC  
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESALTWGVGLALAPALWWGVVC  
PSC

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**FIGURE 251**

GCGACGGGCAGGACGCCCCGTTTCGCCTAGCGCGTGCTCAGGAGTTGGTGTCTGCCTGCGCT  
CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG  
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG  
CCTCAAAGGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCCGACGGCCTGGAAGAGTCG  
GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTTCGTCTAT  
GGAAAAATTGGTCCCATTTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC  
TGGTCCTAATGGAGAACCAGGCCTCCCATGTGAGTGCAGCCAGCTGCGCAAGGCCATCGGGG  
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTGCGC  
GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA  
CGCCCAGCTGTCCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA  
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCGTGTCTTCATCGGCATCAAC  
GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA  
GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT  
CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG  
GAGAACATGTGAGCCTCAGGCTGGGGCTGCCCATTGGGGGCCCCACATGTCCCTGCAGGGTT  
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG  
GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG  
AAAGTGTTCCCTGGGGTGTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA  
ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC  
TATACAATAAAATCTTTAAGTAGTGAGTAGTTAAGTCCAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 252**

MRGNLALVGVLI SLAFLSLLPSGHPQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG  
PTGEKGMGDKGQKGSVGRHGKIGPIGSKGEKGDSDIGPPGPNGEPGLPCECSQLRKAIGE  
MDNQVSQLTSELKFIKNAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAAN  
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVEMVAS  
GGWNDVACHTTMYFMCEFDKENM

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**FIGURE 253**

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG  
CACCAGTGTGTGAGGGGAGCAGGCAGCGGTCTAGCCAGTTCCTTGATCCTGCCAGACCACC  
CAGCCCCCGGCACAGAGCTGCTCCACAGGCACCATGAGGATCATGCTGCTATTACAGCCAT  
CCTGGCCTTCAGCCTAGCTCAGAGCTTTGGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG  
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC  
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA  
GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA  
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCTTCGGCCC  
CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC  
TTTATTAAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT  
ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC  
TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTCTCTTCCCTGTTCTTGT  
AACATTCTTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAACTGCA  
TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCCTGTAGTGT  
CCTACATTAAAAATATAATGTCTCTCTCTATTCCCTCAACAATAAAGGATTTTGCATATGAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 254**

MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK  
ALSQASTDPKESTSPEKRDMDHDFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK  
SSLGTEEQRPL

**Important features:**

**Signal peptide:**

amino acids 1-18

**Tyrosine kinase phosphorylation site.**

amino acids 36-45

**N-myristoylation site.**

amino acids 33-39, 59-65

**Amidation site.**

amino acids 90-94

**Leucine zipper pattern.**

amino acids 43-65

**Tachykinin family signature.**

amino acids 86-92

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**FIGURE 255**

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCCTGTGCCTGCTGTGCC  
CGCGCTGTGCGCCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG  
GAGCCCTGCGGAGAGCTCAAGCGCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC  
CCATAGTTGCTGCAGGAGTGGAGCC**ATG**AGCTGCGTCCTGGGTGGTGTATCCCCTTGGGGC  
TGCTGTTCTGGTCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG  
CTGCTCAGCAAATACCAGCACAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA  
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCCT  
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC  
CTGGGCCACCAGCCTGCTCTGTTCCCCAGCCAGCTCTGTTCCCCAGCCAGTGCGTGTGATGG  
CTGGCTCAGGGTCTCCTCTGGCAGGGGAGGATCCCGGCTCTGTTCTGTTTTGTTTGTGTTT  
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG  
AAACCT**TAG**ACTCCCGGGTTAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACACAG  
GCATGCACCATGGTGCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT  
TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG  
CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA  
ACAACACACGTGGGTTCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC  
TCCACTGGGAACACAGCTCTCAGCCTTTCCACCTGGAGGCAGAGTGGGGAGGGGGCCAGGG  
CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC  
CTTAGCCCGTGTGAGCCTCACTTTCCACTTGGAGAGTCCTTCCTCGCGTGGTTGCCATGACT  
GTGAGATAAGTCGAGGCTGTGAAGGGCCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG  
CTTTGCTAACC GGGAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCCTCCCGGGT  
GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG  
TGGAACCTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG  
GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTCAGCTATGAATGGCTT  
TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAATC  
CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG  
GTGGAGGTGGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC  
AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAAA

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## **FIGURE 256**

MSCVLGGV IPLGLLFLVCGSQGYLLPNVTLLLEELLSKYQHNEHSRVRRAIPREDKEEILML  
HNKLRGQVQPQASNMEYMVSA GSGRRGWHRGWGLGHQPALFPSQLCSPASACDGWLRVSSGR  
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

**Important features:**

**Signal peptide:**

amino acids 1-22

**N-glycosylation site.**

amino acids 27-31, 41-45

**N-myristoylation site.**

amino acids 126-132, 140-146

**Amidation site.**

amino acids 85-89

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**FIGURE 257**

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGG  
GTCTGGGCTGCCCCCTTGTCCTCCTCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGG  
GTATGACTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGC  
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTTCAGGGACCAGCGTCAC  
CCTCCACCATGCAAGATCTCAACACCATGTTGTCTGCAACACATTGACAGCCATTGAAGCCTG  
TGTCTTCTTGGCCCGGGCTTTTGGGCCGGGGATGCAGGAGGCAGGCCCCGACCCTGTCTTT  
CAGCAGGCCCCCACCTCCTGAGTGGCAATAAATAAAATTCGGTATGCTG



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**FIGURE 258**

MGSGPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSYESSFELLEKLCLLLHLPSTGTS  
VTLHHARSQHHVVCNT

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**FIGURE 259**

AATTGTATCTGTGTAATGTTAAAACAAACGAAATAAAATAGAAGGAAAACTTTCTGAGTTT  
CAAAAACAACAGACTAGTACTCTAAAGAACTCTTTAAAACAATTAAGTGTAGGATTGCAGT  
**TATG**ATTGGATATTATTTAATTCTGTTTCTGATGTGGGGTTCCTCCACTGTGTTCTGTGTGC  
TATTAATATTTACCATTGCAGAAGCTTCATTCAAGTGTGAAAATGAATGCTTAGTGGATCTG  
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTTCCTAATCAATGCAGAGTCCCCCTCCC  
CTCCGATTGTTCTAAAT**TAA**TTGAAAGATGTCTGCTGTGGAAAAGGCATGTATTTAAATCTG  
TATGATTCTCAACCATCTTTAGTTGGGAAAGGTCCTTGAAAGCCAATGGAAATACTTTTTTTT  
TTTTCTTGGCACTAATCAAGTGAGTGTTACCTTTTCACTTAGTAGGATGTGTTGTTACGCTA  
GTAAAATAGAAACCTGTGTTTATTCTCAGGTATTTTAGAAACAACAGCCATCATTTTATTTT  
ATGTGTGTGTTCTTGGCTGTATTCATAAATTATATATTTTGGGCTATCAAATATTACTTCAT  
TCAATATAAATAACAATAGTAGAAGTTGTTTACTTAGATATGCTTTCTAGTTGCATTTTCTC  
AGCCTATGTAAGACTACTTTGTTGTAATAGCCTTTGAAATTTACAGTACTGTCTCTCTACTA  
TCTTCAGATTACTTGATTCAAATAAACCAATTATGTTTGTAATTGATATTAATAAAACCAGA  
ATAAAAGTTCATATCTACCC

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**FIGURE 260**

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP  
SDCSK

**Important features:**

**Signal peptide:**

amino acids 1-29

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**FIGURE 261**

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGCCCTTGAGACATCCTT  
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTGTTTGCAGGATGATGGTGGCCCTT  
CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCCTTGACAGCTTTTCTGCCCCCGCCGAGTGATC  
CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG  
AAAAATGTACCCAAGCAACGAGGGCATAACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA  
TCTGTCATGCTGGGAAGATGTCAGACCTACACAAGTGAGTACAAGAGTGCAGTGGGTAACTT  
GGCACTGAGAGTTGAACGTGCCCAACGGGAGATTGACTACATACAATACCTTCGAGAGGCTG  
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA  
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC  
TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA  
ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC  
ATACGGGCATTTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC  
CTGGCAGGGAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTTCATAACCAAGCAACTT  
CTAATGAGATAATCAAATATAACCTGCAGAAGAGGACTGTGGAAGATCGAATGCTGCTCCCA  
GGAGGGGTAGGCCGAGCATTTGGTTTTACCAGCACTCCCCCTCAACTTACATTGACCTGGCTGT  
GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA  
CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTCATGGGATACCCCATGCAGAAGCCAG  
GATGCTGAAGCCTCATTCCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA  
GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC  
CCAACCTTGTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCCAAGAGAT  
AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAA  
GCTGCCTCTGAAGTAATGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTT  
TACAGGACAGTGAGGCTATAGCCCCCTTCACAATATAGTATCCCTCTAATCACACACAGGAAG  
AGTGTGTAGAAGTGGAAATACGTATGCCTCCTTTCCCAAATGTCACTGCCTTAGGTATCTTC  
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCCAA  
CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACT  
GCTCCCCAGCATTTACTGTAACCTCTGCCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGC  
CCCTAATATTACCACTGGCTTTTCTCTCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT  
CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT  
CTTTTCTTTTCTTTTTTTTGTAGACAAGGTCTCACTATGTTGCCAGGCTGGTCTCAAACCTCC  
AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC  
CACACCTGGCTTAAATACTATTTCTTATTGAGGTTTAACTCTATTTCCCTAGCCCTGTC  
CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT  
CCAGGTGTGGAGTGTGTTGCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG  
TCTTTACAGCTGTCATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC  
TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT  
TGTTACCTACTCTTATAGTCAATGCGTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC  
TTTAGCCAGTTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC  
AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTTGTCTTGTCTCTCTGT  
TTCTCTCTTTCTGCTTTAAATTCAATAAAAGTGACACTGAGCAAAAAAAAAAAAAA

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**FIGURE 262**

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQE  
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL  
QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNSPKVYLLIGSRNNTV  
WEFANIRAFMEDNTKPAPRKQILTLWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED  
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKEPGTLGVEHSWDT  
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH  
YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK



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**FIGURE 264**

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK  
QYQIRIRKEKPQQHNFTHRLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ  
REHRSMRANVELDHATLVRFPDCRAFIVWLANGDTLRVFKMTKREDGGYTFTATPEDFPKK  
HKAPVIDIGIANTGKFIMTASSDTTVLIWLSLKGQVLSTINTNQMNNTHAHVSPCGRFVASC  
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV  
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH  
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ  
AQETLKSLGALKK

**Important features:****Signal peptide:**

amino acids 1-25

**N-glycosylation site.**

amino acids 76-80, 92-96, 231-235, 289-293, 378-382, 421-425

**Beta-transducin family Trp-Asp repeat protein.**

amino acids 30-47, 105-118, 107-119, 203-216, 205-217, 296-308

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**FIGURE 265**

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG  
CAGTGTTTTGCCTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCC  
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT  
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT  
GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA  
AGCACCACACCTGTCCTTGCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTAC  
CGCTGCTCCATGGACTTGAAGAACATCAATTTTTAGGGCGCTTGCTGGTCTCAGGATACCCA  
CCATCCTTTTCCTGAGCACAGCCTGGATTTTTATTCTGCCATGAAACCCAGCTCCCATGAC  
TCTCCCAGTCCCTACACTGACTACCCTGATCTCTCTTGTCTAGTACGCACATATGCACACAG  
GCAGACATACTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTACAGCTTGAGG  
CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTTCCCTGCTCAGGCTGCCAGAGAGGTGGTA  
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTCTTTCCTGGGCCCTG  
CCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTTGGGCACAGGCTCTTGGGT  
GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG  
ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTCAGACCACAGAC  
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA  
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA  
CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT  
TAACCACTGAAGCCCCCAATTCCCACAGCTTTTCCATTAAAATGCAAATGGTGGTGGTTCAA  
TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTTCCTTAAACAACCTCCTTTCCA  
AGGATCAGCCCTGAGAGCAGGTGGTGACTTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG  
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTACAGACCAGGGAGG  
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAAA



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**FIGURE 266**

MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHP  
GSHKVPFFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

**Signal peptide:**

amino acids 1-19

**Tyrosine kinase phosphorylation site:**

amino acids 88-95

**N-myristoylation sites:**

amino acids 33-39, 35-41, 46-52

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**FIGURE 267**

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCCTTTC  
CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC  
TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG  
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA  
GCAAAGGAGCTATGGGAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT  
CCTCTGTGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG  
TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT  
TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAAGTTCTATGGTCCACAAAGGCGGAAGAT  
GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACCTTCTTCCGAGCCTGGAACGGAG  
GCTTCTCTGGAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA  
GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT  
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAATGAT  
TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTTCATGGGATGTATT  
GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA  
TTAATGTATTTTAATATTCTGTTTAGGCCCCTAAGGCAAATAGCCCCAAAACAAGACTGA  
CAAAAATCTGAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA  
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG  
TGAGCAAGTCACTTGAGGTCGGGAGTTCGAGACCAGCCTGAGCAACATGGCGAAACCCCGTC  
TCTACTAAAAATACAAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG  
GGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA  
CACCACTGTATTCAGCCTGGGTGACTGAGACTCTAACTAA

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**FIGURE 268**

MSFLQDPSFFTGMWSIGAGALGAAALALLANTDVFLSKPQKAALEYLEDIDLKTLEKEPR  
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF  
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEFGFILGGVFV  
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

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**FIGURE 269**

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCCG  
GGCCAGGTGCCCCGTCGCAGGTGCCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA  
AGCCCCTTCCTCGGCGCTGCCAACCCGCCACCCAGCCC**ATG**GGCGAACCCCGGGCTGGGGCTG  
CTTCTGGCGCTGGGCCTGCCGTTCTTGCTGGCCCGCTGGGGCCGAGCCTGGGGGCAAATACA  
GACCACTTCTGCAAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATG  
GCAACCTGCGTCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTTGGCTGCCTTG  
CTCCTGGCTGTGGGGCTGGCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGG  
CACCTACCGGCCCAGTAGCGAGGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCCCTCAGG  
ACTCCAAGGAGACGGTGCAGGGCTGCCTGCCCATC**TAGGT**CCCCCTCTCCTGCATCTGTCTCC  
CTTCATTGCTGTGTGACCTTGGGGAAAGGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAG  
TGCTTAATAGCAGGGAAGAAGGTACTTCAAAGACTCTGCCCTGAGGTCAAGAGAGGATGGG  
GCTATTCACTTTTATATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAAAAAAA

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**FIGURE 270**

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSTSSSSDGNLRPEAITAIIV  
VFSLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

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**FIGURE 271**

AATATATCATCTATTTATCATTAATCAATAATGTATTCTTTTATTCCAATAACATTTGGGTT  
TTGGGATTTTAATTTTCAAACACAGCAGAATGACATTTTTTCTGTCACTATTATTATTGTTG  
GTATGTGAAGCTATTTGGAGATCCAATTCAGGAAGCAACACATTGGAGAATGGCTACTTTCT  
ATCAAGAAATAAAGAGAACCACAGTCAACCCACACAATCATCTTTAGAAGACAGTGTGACTC  
CTACCAAAGCTGTCAAAACCACAGGCAAGGGCATAGTTAAAGGACGGAATCTTGACTCAAGA  
GGGTTAATTCTTGCTGAAGCCTGGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG  
ATTGTAAATTTAAGGCAAATACACATATTAGTATTACCTTAGTGTAATGTATCCCTGTCATA  
TATACAATAAGGTGAAATTATAAGTACCCTATGCAGTTGGCTGGACAGTTCTAAATTGGACT  
TTATTAATTTTAAAAATCAGTAACTGATTTATCACTGGCTATGTGCTTAGATCTACAGGAGA  
TCATATAATTTGATACAAATAAAAGAAAAGTGTTCTCTCCCCTTACAGAATTGACATTTTAA  
ATGCGATACAGTTAGAATAGGAAATATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA  
AGAAGGGAAAATGTTGCCAAGGAAAAAAAAA

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**FIGURE 272**

MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK  
GIVKGRNLDSRGLILGAEAWGRGVKKNT





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**FIGURE 274**

MGLFRGFVFLLVLCLLHQSNSTFIKLNNGFEDIVIVIDPSVPEDEKIIIEQIEDMVTTASTY  
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKKHADVIVAPPTLPGRDEPYTKQFTEC  
GEKGEYIHFTPDLLLGGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR  
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVE  
FCNEKTHNQEAPSLQNIKCNRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV  
LDKSGSMGGKDRNLNRMNQAAKHFLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM  
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTGDEDNTASSCIDEVKQSGAIVH  
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT  
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG  
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNKDVNSFPSPMIVYAEILQG  
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNMGVYSRYFTAYTENGRYSLKVRAG  
GANTARLKLRPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRTASGGAFVVSQV  
PSLPLPDQYPPSQITDLDATVHEDKIILTWAPGDNFVGVQRYIIRISASILDRDSFDD  
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSANIAQVTLFIP  
QANPDDIDPTPTPTPTPTPDKSHNSGVNISTLVLSVIGSVVIVNFILSTTI

**Signal peptide:**

amino acids 1-21

**Putative transmembrane domains:**

amino acids 284-300, 617-633

**Leucine zipper pattern.**

amino acids 469-491, 476-498

**N-glycosylation site.**amino acids 20-24, 75-79, 340-344, 504-508, 542-546, 588-592,  
628-632, 811-815, 832-836, 837-841, 852-856, 896-900

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**FIGURE 275**

CTCCTTAGGTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAGACCATACGTCCCCG  
GGCAGGGGTGACAAACAGGTGTCATCTTTTTGATCTCGTGTGTGGCTGCCTTCTTATTTCAAGGAAAG  
ACGCCAAGGTAAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCTAACCTTCCCTTCTTGAACC  
CCCAGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACTT  
GTGGTTGGAGGAGAGAACCCTTTGTGGGGCTGCGTTCTCTTAGCAGTGCTCAGAAGTGACTTGCCTGA  
GGGTGGACCAGAAGAAAGGAAAGGTCCCCTCTTGCTGTTGGCTGCACATCAGGAAGGCTGTGATGGG  
AATGAAGGTGAAAACCTTGGAGATTTCACTTCAGTTCATTGCTTCTGCCTGCAAGATCATCTTTAAAA  
GTAGAGAAGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCAGAACTCGTTCTAGAAGGAAATGGATG  
CAAGCAGCTCCGGGGGGCCCCAAACGCATGCTTCTGTGGTCTAGCCCAGGGAAGCCCTTCCGTGGGG  
GCCCCGGCTTTGAGGGATGCCACCGTTCTGGACGCATGGCTGATTCTGAATGATGATGGTTCCGCC  
GGGGGCTGCTTGCCTGGATTTCCCGGGTGGTGGTTTGGTGGTGCCTCTGCTGTGCTATCTCTGT  
CCTGTACATGTTGGCCTGCACCCAAAAGGTGACGAGGAGCAGCTGGCACTGCCAGGGCCAACAGC  
CCCACGGGGAAAGGAGGGGTACCAGGCCGCTCTTCAGGAGTGGGAGGAGCAGCACCGCAACTACGTGA  
GCAGCCTGAAGCGGCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGAGCAGCTCAACGAA  
TGGGCAGTACCAAGCCAGCGATGCTGCTGGCCTGGGTCTGGACAGGAGCCCCCAGAGAAAACCCAG  
GCCGACCTCCTGGCCTTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGG  
CCACAGAGTATGCAGCAGTGCCTTTCGATAGCTTTACTCTACAGAAGGTGTACCAGCTGGAGACTGG  
CCTTGCCACCTCCCGGAGGAGAAGCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGGAAAGCCATT  
GAATCAGCCTTGGAGACCCTGAACAATCCTGCAGAGAACAGCCCCAATCACCGTCTTTACACGGCCT  
CTGATTTTCATAGAAGGGATCTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAA  
AGGGGACCACAAACACGAATTCAAACGGCTCATCTTATTTTCGACCATTACGCCCCATCATGAAAGTG  
AAAAATGAAAAGCTCAACATGGCCAACACGCTTATCAATGTTATCGTGCCTCTAGCAAAAAGGGTGG  
ACAAGTTCCGGCAGTTTCATGCAGAATTTTCAGGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCT  
CACTGTTGTTTACTTTGGGAAAGAAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAA  
GCTGCCAACTTCAGGAACCTTACCTTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTG  
ATGTTGGAGCCCGCTTCTGGAAGGGAAGCAACGTCTCTCTTTTCTGTGATGTGGACATCTACTT  
CACATCTGAATTCCTCAATACGTGTAGGCTGAATACACAGCCAGGGAAGAGGATTTTATCCAGTT  
CTTTTCAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCCTCCTTGGAAACAGC  
AGCTGGTCATAAAGAAAGGAACTGGATTTTGGAGAGACTTTGGATTGGGATGACGTGTGAGTATCG  
GTCAGACTTCATCAATATAGGTGGGTTTGATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCAC  
CTTTATCGCAAGTATCTCCACAGCAACCTCATAGTGGTACGGACGCTGTGCGAGGACTCTTCCACC  
TCTGGCATGAGAAGCGCTGCATGGACGAGCTGACCCCGAGCAGTACAAGATGTGCATGCAGTCCAA  
GGCCATGAACGAGGCATCCACGGCCAGCTGGGCATGCTGGTGTTCAGGCACGAGATAGAGGCTCAC  
CTTCGCAACAGAAACAGAAAGACAAGTAGCAAAAAACATGAATCCAGAGAAGGATTTGTTGGGAGA  
CACTTTTCTTTCTTTTCAATTACTGAAAGTGGCTGCAACAGAGAAAAGACTTCCATAAAGGACG  
ACAAAAGAATTGGACTGATGGGTGAGAGATGAGAAAGCCTCCGATTTCTCTCTGTTGGGCTTTTAC  
AACAGAAATCAAAATCTCCGCTTTGCCTGCAAAAGTAACCCAGTTGCACCCTGTGAAGTGTCTGACA  
AAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTGTGGAGGTTTGTGAGGTGTTTACAATACACT  
GAGACCTGTTGTTTTGTGTGCTCATTGAAATATTATGATTTTAAGAGCAGTTTTGTAAAAAATTCAT  
TAGCATGAAAGGCAAGCATATTTCTCCTCATATGAATGAGCCTATCAGCAGGGCTCTAGTTTCTAGG  
AATGCTAAAATATCAGAAGGCAGGAGAGGAGATAGGCTTATTATGATACTAGTGAGTACATTAAGTA  
AAATAAAATGGACCAGAAAAGAAAAGAAACATAAATATCGTGTCAATTTTCCCAAGATTAACCA  
AAAATAATCTGCTTATCTTTTGGTTGCTCTTTTAACTGTCTCCGTTTTTTTCTTTTATTTAAAAAT  
GCACTTTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTACCACTTTGCAAGCCTTACAAGAGA  
GCACAAGTTGGCCTACATTTTTATATTTTTTAAGAAGATACTTTGAGATGCATTATGAGAACTTTCA  
GTTCAAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATGCTGATTCTGTCAGGCACTGAAT  
GTCAGGCATTGAGACATAGGGAAGGAATGGTTTGTACTAATACAGACGTACAGATACTTTCTCTGAA  
GAGTATTTTTCGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATGACACTTTCTGCTTTACAGAA  
AAGGAACTCATTCACTGGTGTATCTGTGATGTACCTAAAAGTCAGAAACCACATTTTCTCCTCA  
GAAGTAGGGACCGCTTCTTACCTGTTTAAATAAACCAAAGTATACCGTGTGAACCAAACAATCTCT  
TTTCAAACAGGGTCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAATGGAGAAAATATATATAT  
ATATATATATATTGTGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATGGAAGTTTTTGTCTACAT  
GTTATCCACCCAGGCCAGGTGGAAGTAAGTGAATTTTAAATTAAGCAGTTCTACTCAATCA  
CCAAGATGCTTCTGAAAATTCGATTTTTATTACCATTTCAAACATTTTTTTAAAAATAAATACAGTTA  
ACATGAGAGTGGTTTCTTCATTCATGTGAAAATTATTAGCCAGCACCAGATGCATGAGCTAATTATCT  
CTTTGAGTCTTGTCTGTTTGTCTCACAGTAACTCATTTGTTTAAAAGCTTCAAGAACATTCAAGC  
TGTGGTGTGTTAAAAAATGCATTGTATTGTAATTTGTAAGTGTGTTTATGAAATTTAAATTAACAC  
AGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAATATGATTTGTGGATATGAA

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**FIGURE 276**

MMMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQ  
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL  
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPVRKDKRDELVEAIES  
ALETLNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP  
MKVKNEKLNMAN TLINVI VPLAKRVDKFRQFMQNFREMCIEQDGRVH LTVVYFGKEEINEVK  
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLN TCR  
LNTQPGKKVFYPVLFSQYNPGIIYGHHD AVPPLEQQLV IKKETGFWRDFGFGMTCQYRSDFI  
NIGGFDL DIKGWGGEDVHLYRKYLHSNLIVVRTPVRGLFHLWHEKRCMDELTPEQYKMCMQS  
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

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**FIGURE 277**

GAAAGAATGTTGTGGCTGCTCTTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACC  
AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT  
ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA  
GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT  
ATCATTCTGGTTTGTGGTTACAGACCCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC  
AATCAGCCATAAGAATGAAÇAAGAACCGGATCAACAATGCCTTCTTTCTAAATGACCAAACCT  
CTGGAATTTTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG  
GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCACTACTGATTTTAT  
CAGGGATCTGGCAACGTAGAAGAAAGAAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT  
AAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCCTCTGATCCCCTGGACATGAAGGG  
GGGCATATTAATGATGCCTTCATTGACAGAGGATGAGAGGCTCACCCCTCTCTGAAGGGCTGT  
TGTTCTGCTTCCTCAAGAAATTAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA  
CCAAGAGCAGATCATATATTTTGTTCACCATTCTTCTTTTGTAAATAAATTTTGAATGTGCT  
TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC  
TCAAATATTCTAAATATTTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG  
TAGTTATTGATTTAAGCATTTTGTAGAAATAAGATCAGGCATATGTATATATTTTTCACACTTC  
AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT  
TGAAAATGGATCCTTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG  
TGAGAAGTAATTATTGTAAATGGATGGATAAAAATGGAATTACTCATATACAGGGTGGAATT  
TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC  
AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG  
TAATAATCATCTCTTTTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 278**

MLWLLFFLVTAIHAE LCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP  
NREATEISHVLLCNVTQRVSFWFVVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE  
FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC  
ENMITIENGIPSDPLDMKGGILMMPS

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**FIGURE 279**

AACTCAAACCTCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG  
GTGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTC**ATGT**  
ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGG  
CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC  
TCGGTTAAAATGCACCTTTCTCCAGCTTTGCCCCCTGTGGGTGATGCTCTAACAGTGACCTGGA  
ATTTTCGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC  
CAACCCATGAGTGGGCGGTTTAAGGACCGGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA  
TGCCTCCATCCTTCTCTGGAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA  
AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA  
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT  
AATAGTAATTGTAAGTGGTCCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC  
ATAAAGTGGTGGAGATAAAATCAAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT  
GTTTATTTAGAAAGACACAGAC**TAA**CAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA  
GAACCCTAGTATTTCTTGAAGTTAATGGAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT  
TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC  
AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTTCTAGA  
GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTGCCCTTAA  
GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC  
AATTTGTCTGTTACATTTTCCTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA  
ATGTGTTTACTCTCTTTCCCTTCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG  
TTTCTGATTAAACAGTAAATCCTAAATTCAAACCTGTTAAATGACATTTTTATTTTTATGTCTC  
TCCTTAACATATGAGACACATCTTGTTTTACTGAATTTCTTTCAATATTCAGGTGATAGATT  
TTTGTCG

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**FIGURE 280**

MYGKSSTRAVLLLLGIQLTALWPAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT  
WNFRPLDGGPEQFVFYYHIDPFQPMGRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ  
VKNPPDVGVI GEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVL FQHYRKKRWAER  
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

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**FIGURE 281**

GCATTTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACCATGAAGTTCTTAGCAGTCCTGGT  
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG  
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT  
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG  
TAAAGACATTCCAGTTTTACCCAAATGGGTTGGGGATCTCCCGAATGGTAGAGTGTGTCCCT  
GAGATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACATTCATGCTTCCTGTGATTC  
ATCCAAC TACTTACCTTGCCTACGATATCCCCTTTATCTCTAATCAGTTTATTTCTTTCAA  
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA



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**FIGURE 282**

MKFLAVLVLLGVSI FLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTAT  
TAASTTARKDIPVLPKWVGDLPNGRVCP

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**FIGURE 283**

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC  
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAATGC  
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA  
GTGTCCTGGGTGAGGGACGCAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC  
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG  
GACAGTTCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGGCCAGTCCAGGGTGGGGGGCG  
GCAAACCTCCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCCAGCTCCT  
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAGTTAAAACCACAGGCTGG  
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA  
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTTACCACATTAGCAATTAAAACTGAGAAAT  
GGGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT  
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA  
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG  
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT  
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA

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**FIGURE 284**

MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG  
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ

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**FIGURE 285**

GTC**ATG**CCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTGACCCGGCCTGCCTCA  
GCGGCCCCCATGGGCGGCCAGAACTGGCACAGCATGAGGAGCTGACCCTGCTCTTCCATGG  
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCACGGAGGGACGGCTGACAA  
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTCAGC  
CGGGGCCGGGATGCAGCCCAGGAACTTCGGGCAAGCCTGTTGGAGACTCAGATGGAGGAGGA  
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCCAGGCACAGA  
AGGTGCTACGGGACAGCGTGCAGCGGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGGCCCT  
GCCTACCGAGAATTTGAGGTCTTAAAGGCTCACGCTGACAAGCAGAGCCACATCCTATGGGC  
CCTCACAGGCCACGTGCAGCGGCAGAGGCGGGAGATGGTGGCACAGCAGCATCGGCTGCGAC  
AGATCCAGGAGAGACTCCACACAGCGGCGCTCCCAGCC**TGA**ATCTGCCTGGATGGAAGTGA  
GACCAATCATGCTGCAAGGAACACTTCCACGCCCCGTGAGGCCCTGTGCAGGGAGGAGCTG  
CCTGTTCACTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGAGCAGAGACAGAC  
GCAGGCGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA  
CCCTTTCATGCCTACACACCCCTCATTAAAGCAGAGTCGTGGCATTTCAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 286**

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK  
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK  
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ  
IQERLHTAALPA

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**FIGURE 287**

GGCAACATGGCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT  
CCTGGTGATCACCTTACTCCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA  
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC  
TGGACAGAAGTCAATGCCTTGAAGGAAATTCAAGCCCTGCAGACAGTCTGTCTCCGAGGCAC  
TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG  
AAGACTGCATTTCCAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC  
CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA  
CATGGTCACGGAAGGCAAGTTTGTGACGTCAACGGAATCGCTATCTCCTTCCTCAACTGGG  
ACCGTGCACAGCCTAACGGTGGCAAGCGAGAAAACCTGTGTCCTGTTCTCCCAATCAGCTCAG  
GGCAAGTGGAGTGATGAGGCCTGTCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC  
TAAATTAGGTCTTTCTCCAATGTGTCCTCCAAGCAAGATTCATCATAACTTATAGGTTTCATGA  
TCTCTAAGATCAAGTAAAAATCATAATTTTTTACTTATTAAAAAATTGCAACACAAGATCAAT  
GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT  
TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT  
AAACAGACTAAAATCTTTCTCTCTAGTCTTTCTCACTTGTAACAAACCCAGTTTGTTTTCAA  
AAATCACAGTAGCAATGCAACTCATCACTCTAGAAAAGCAAGCTTAGGCTACCTGAAAGATT  
TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATCCCTACATCAGAGACTCTAGGT  
GCTATATAATCCAAAACTTTTCAGCCTGTTGCTCATTCTGTCCCATGCTGGCAATAATACC  
TTGTCAGCCCATTACCCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGATCTTGCTCT  
GCCATATCAGAACACAAACCCCTGAAGAGGTTCTGATTTGATTTTTTTTTTTCTTCATGCC  
TACCCTTTTTTTTGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTTGAT  
CAATTTTCATTCCCACCATTGCATTACAACCTCTAACTTAAATGGGTAACCCTAAGGCATAT  
CAAAGAAGCAGATTGCATGATAAACGGAAATAGAAAAAAGAACCTACATTTATTTTGCTTT  
AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCCCTTTTTTACATTT  
TCGTATATTTATTTTTTTTAGCCATCATTATATGTTTAAAGTCTATTATGGGCAACCAATCTT  
TGGAAGCTGAAAACCTGAATTTAAAGAATGCTATCTTGGAATTTGCATACGTCTGTGCAATT  
TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT  
TAATATCAAATTACAAAGTTTAGACTTGGAGGGAAATGGGCTTTTTTAGAAGCAAACAATTTT  
AAATATATTTTGTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT  
CCCACTTTGCAAACCTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTTCATTGCTCA  
ATAATAAAGCCTGAATTCTGATCAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 288**

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGD LKTQIEKLWT  
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ  
DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQ GK  
WSDEACRSSKRYICEFTIPK

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**FIGURE 289**

GCGAGGACCGGGTATAAGAAGCCTCGTGGCCTTGCCCGGGCAGCCGCAGGTTCCCCGCGCGC  
CCCGAGCCCCCGCGCCATGAAGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCCTGCA  
GCTCCGCTGCTGCTTTCTTAGTGGGCTCGGCCAAGCCTGTGGCCCAGCCTGTCGCTGCGCTG  
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCTGGCCAACCCCCTCGGCACCCTCAACCCGCT  
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACCACCTCATAGAGGGCTCCCAGAAGT  
GTGTGGCTGAGCTGGGTCCCCAGGCCGTGGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG  
GCCCTGACAGTGTTTGGCTGAGCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC  
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCTTCCCCGGCCCCCT  
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAA



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**FIGURE 290**

MKLAALLGLCVALSCSSAAAFVGSAPVAPVAALESAAEAGAGTLANPLGTNLPLKLLLS  
SLGIPVNHLEGSQKCVNELGPQAVGAVKALKALLGALTVEFG

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**FIGURE 291**

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT  
CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGTCTCCTG  
GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCAGTCCTCAGTCGCCAGAGACCCCAGCCCC  
TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGG  
CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGGCAGCAGCTT  
GCCAAGGAGACTTCAAACCTTCGGATTACAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG  
CAACATGGTCTTCTCTCCATTTGGCATGTCTTGGCCATGACAGGCTTGATGCTGGGGGCCA  
CAGGGCCGACTGAAACCCAGATCAAGAGAGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG  
CCCGGGCTCCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCTCTCCCGCAACCTGGAAGT  
GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT  
TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCCTGCTATGAATTTTCGCAATGCCTCA  
CAGGCCAAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGGAAAATTCCCAAAGT  
GTTTGATGAGATTAATCCTGAAACCAAATTAATTCTTGTGGATTACATCTTGTTCAAAGGGA  
AATGGTTGACCCCATTTGACCTGTCTTACCAGAAGTCGACACTTTCCACCTGGACAAGTAC  
AAGACCATTAAAGGTGCCCATGATGTACGGTGCAAGGAAAGTTGCCTCCACCTTTGACAAGAA  
TTTTCGTTGTCATGTCCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCCTCA  
TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA  
TGGCTCAGAAACATGAAAACCAGAAACATGGAAGTTTTCTTTCCGAAGTTCAAGCTAGATCA  
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTACCCCTTG  
CTGACCTTAGTGAACCTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA  
ACAGTGATTGAAGTTGATGAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTCAGAAATTAC  
TGCTTATTCCATGCCTCCTGTATCAAAGTGGACCGGCCATTTCAATTCATGATCTATGAAG  
AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTATAATTCAGG  
ACATGCATAAGCACTTCGTGCTGTAGTAGATGCTGAATCTGAGGTATCAAACACACACAGGA  
TACCAGCAATGGATGGCAGGGGAGAGTGTTCTTTTGTCTTAACTAGTTTAGGGTGTCTC  
AAATAAATACAGTAGTCCCACTTATCTGAGGGGGATACATTCAAAGACCCCAGCAGATGC  
CTGAAACGGTGGACAGTGCTGAACCTTATATATATTTTTTCTTACACATACATACCTATGAT  
AAAGTTAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA  
TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACCTGATTATAGAGAAGGCTA  
CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAATTCA  
CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCCATCCCACTACTCAGAATGGCATGC  
TGCTTAAGACTTTTAGATTGTTTATTTCTGGAATTTTTTCATTTAATGTTTTTGGACCATGGT  
TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAA  
GCATTAAATTGATACATATTTTTTAAAAA

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**FIGURE 292**

MKVVPSLLLSVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEDEQEASEEKAGE  
EEKAWLMASRQQLAKETSNFGFSLLRKISMRHDGNMVFSPFGMSLAMTGLMLGATGPTETQI  
KRGLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF  
DTECVPMNFRNASQAKRLMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTFFDP  
VFTEVDTFHLDKYKTIKVPMMYGAGKFASTFDKNFRCHVLKLPYQGNATMLVVLMEKMGDHL  
ALEDYLTDDLVTWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIIRIFSPFADLSELSA  
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF  
LGRVVNPTLL

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**FIGURE 293**

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGACATGAG  
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG  
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG  
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGCTGTTCCC  
TGTCCAGAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAGGGCAGGGGCCCCA  
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCTTGAGTCCC  
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC  
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGGAGGAAGACCAAGACCACA  
TCTACCACCCCCAGTAGGGCTCCAGGGGCCATCACTGCCCCCGCCCTGTCCCAAGGCCCAGG  
CTGTTGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCCAGCAGGCAAA  
AAAAAAAAAAAAAAAAA

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**FIGURE 294**

MRRLLLVTSLVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL  
FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE  
RPRLWVMPNHQVLLGPEEDQDHIYHPQ

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**FIGURE 295**

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG  
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGC  
TGTTTCTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAA  
TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC  
TAGTGCAATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTATCTACCAGACCTTCT  
GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCAATGAGAATGACATG  
CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC  
AGAGGGGGACGGCAACTGGGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG  
ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG  
CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC  
TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT  
ATGGAGAAGGAAAGTGTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTTTGGC  
GACGCCCAGAAAACAGCATCTTATTACTCACCTATGGCCAGCGGGAATTCAGTGCGGGATT  
TGTTCAAGTTCAGGGTATTTAATAACGAGAGAGCAGCCAACGCCTTGTGTGCTGGAATGAGGG  
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT  
CCCCAGCAGTGTGGAGATTTTCTGGTTTTGATTGGAGTGGATATGGAATCATGTTGGTTA  
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTTTGTG  
GGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAACAACCTACCCA  
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA

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**FIGURE 296**

MNQLSFLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN  
GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG  
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI  
YQKYPVKYGEGKCWTDNGPVIPVVYDFGDAQKTASYYSPTYGQREFTAGFVQFRVFNNERAAAN  
ALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGTHVGYSRSSREITEAAVLL  
FYR

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**FIGURE 297**

GCGGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC  
CACGAGGCTGCCGCATCCTGCCCTCGGAACA**ATG**GGGACTCGGCGCGCGAGGTGCTTGGGCCC  
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCGCCCATGAAAGCGCAGCC  
ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACCTCCAGTGCTAACTCAAC  
AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC  
CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG  
GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC  
TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG  
TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACCTATGCAT  
TCTGAAGCAAAGAAAGGATCAAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAC  
GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC  
GGTATCGAACCATAGATGAACATGATGCCATCATT**TAA**GGAAATCCATGGACCAAGGATGGA  
ATACAGATTGATGCTGCCCTATCAATTAATTTTGGTTTATTAATAGTTTAAAACAATATTCT  
CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA  
AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTGAATAAACATCTGGATCTTATAGACCGT  
TCATACAATGGTTTTAGCAAGTTCATAGTAAGACAAACAAGTCCTATCTTTTTTTTTTGGCT  
GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA  
TGCCATCTGGGCATACAATAAGAAGTTTGTACAGCACTCAGGATTTTGGGTATCTTTTGT  
AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA  
CAGAAATTATACAATCAAACCTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG  
TGCTTTAAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC



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**FIGURE 298**

MGLGARGAWAALLLGTQLQVLALLGAAHESAAMAASANIENSGLPNSSANSTETLQHVP  
SDH  
TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSV  
SQN  
TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLT  
LGVL  
SILYIG  
CKMYYSRRGIRYRTIDEHDAII

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**FIGURE 299**

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG  
TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCCAGCGATGGCGACCCTGTGGGGAGGC  
CTTCTTCGGCTTGGCTCCTTGCTCAGCCTGTCGTGCCTGGCGCTTTCCTGCTGCTGCTGGC  
GCAGCTGTCAGACGCCGCCAAGAATTCGAGGATGTCAGATGTAAATGTATCTGCCCTCCCT  
ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT  
CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA  
ATGCAAATATGAAGAAAGAAGCTCTGTCACAATCAAGGTTACCATTATAATTTATCTCTCCA  
TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG  
CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT  
TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG  
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCCAAGAGCAGCGAAAGTCTGTCTTTGACCGG  
CATGTTGTCCTCAGCTTAATTGGGAATTGAATTCAGGTGACTAGAAAGAAACAGGCAGACAA  
CTGGAAAGAACTGACTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTTACCAACT  
GTTGCTGGAAGATTCAAACTGGAAGCAAAAACCTTGCTTGATTTTTTTTTCTTGTTAACGTA  
ATAATAGAGACATTTTTAAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTCCTATTTG  
TGACTTTTACTAATAAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA  
AGCACTCTCTTTTTCACCACATAGTTTTAACTTGACTTTCAAGATAATTTTCAGGGTTTTTG  
TTGTTGTTGTTTTTTGTTTGTGTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT  
AACAACTTTTTTCAAGTCACTTTACTAAACAACTTTTTGTAAATAGACCTTACCTTCTATTT  
TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG  
ACTTTTGCAGTCACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT  
CTAAAATGCCTGGTGGCTTTTCACAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG  
CAATGCATCCTAGAACAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG  
GTGTGTGTGGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT  
TGCAATAAAGAAATTTTATTTTAAACCCAAGCCTCCCTGGATTGATAATATATACACATTTG  
TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT  
AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT  
TCTTCCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTGAACATCAA

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**FIGURE 300**

MATLWGGLRLGSLLSLCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENS  
GHIYNKNIS  
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTII IYLSILG  
LLLLLYMVYLT  
LVEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLA  
RSRANVLNKVEYAQQRWKLQVQEQ  
RKSVFDRHVVL

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**FIGURE 301**

GCACCTGCGACCACCGTGAGCAGTCATGGCGTACTCCACAGTGCAGAGAGTCGCTCTGGCTT  
CTGGGCTTGTCTGGCTCTGTGCTGCTGCTGCCCAAGGCCTTCCTGTCCCGCGGGAAGCGG  
CAGGAGCCGCCGCCGACACCTGAAGGAAAATTGGGCCGATTTCCACCTATGATGCATCATCA  
CCAGGCACCCTCAGATGGCCAGACTCCTGGGGCTCGTTTCCAGAGGTCTCACCTTGCCGAGG  
CATTTGCAAAGGCCAAAGGATCAGGTGGAGGTGCTGGAGGAGGAGGTAGTGAAGAGGTCTG  
ATGGGGCAGATTATTCCAATCTACGGTTTTGGGATTTTTTTATATATACTGTACATTCTATT  
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAATTGAAAATCTAATATGGCGATAAAAA  
TCATTGTCTACATTAAACTTCTTATAGTTCATAAAATTATTTCAAATCCATCATCTCTTTA  
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTTAGTTTCACATAAGAATG  
TTTACTCAATGTTTAAGTGTTTTGCCCCAAAATTCACAACCTAACAAGGCAGAACTAGGACTT  
GAACATGGATCTTTTGGTTCTTAATCCAGTGAGTGATACAATTCAATGCACTCCCCTGCCA

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**FIGURE 302**

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPTPEGKLGRFPPMMHHHQAPSDGQT  
PGARFQRSHLAEAFKAKGSGGGAGGGGSGRGLMGQIIPYGFIFLYILYILFKVSRIILI  
ILHQ

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**FIGURE 303**

CGGCTCGAGTGCAGCTGTGGGGAGATTTTCAGTGCATTGCCTCCCCTGGGTGCTCTTCATCTT  
GGATTTGAAAGTTGAGAGCAGCATGTTTTTGGCCACTGAAACTCATCCTGCTGCCAGTGTTAC  
TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTCCCCGCCTGAGCTAACAGTCCATGTG  
GGTGATTCAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT  
AGACTGGACTCTGTCAACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA  
ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC  
AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA  
AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG  
AGGAGCCCAAAGAGCTCATGGTCCATGTGGGTGGATTGATTGAGATGGGATGTGTTTTCCAG  
AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA  
GGAGATTGTATTTTCGTTACTACCACAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG  
GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG  
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGGAACCT  
GGTGTTCAGAAAACCATTTGTGCTGCATGTGAGCCCGGAAGAGCCTCGAACACTGGTGACCC  
CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTC  
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA  
GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG  
AAAAACCCTGCCATTTTGAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA  
CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA  
CCCAGTTTGGCCTTCTCTGAGGTGAGATCGGAACAACCTCACTTGAAAAAAAGTCAGGTGGGG  
GAATGCCAAAAACACAGCAAGCCTTTTTGAGAAGAATGGAGAGTCCCTTCATCTCAGCAGCGG  
TGGAGACTCTCTCCTGTGTGTGTCCTGGGCCACTCTACCAGTGATTTGAGACTCCCGCTCTC  
CCAGCTGTCCTCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG  
CAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGC  
CTCTGGAGTGGGACACTGGCCCTGGGAACCAGGCTGAGCTGAGTGGCCTCAAACCCCCGTT  
GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA  
AAACCAACCCAAATCAA

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**FIGURE 304**

MFCPLKLILLPVLLDYSLGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLS PG  
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES  
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY  
HKLMSVEYSQSWG HFQNRVNLVGDI FRNDGSIMLQGVRES DGGNYTCSIHLGNLVFKKTIV  
LHVSPEEPRTLVT PAALRPLVLGGNQLV IIVGIVCATILLPV LILIVKKT CGNKSSVNSTV  
LVKNTKKTNPEIKEKPCHFERCEGEKHIYSPIIVREVIEEEEPSEKSEATYMTMHPVWPSLR  
SDRNNSLEKKSGGGMPKTQQAF

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**FIGURE 305**

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG  
GTTCTACCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGG  
AAACTACATTTTGCAGGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCCATGCA  
GGATGAAGATGGATACATCACCTTAAATATTAAAACTCGGAAACCAGCTCTCGTCTCCGTTG  
GCCCTGCATCCTCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGG  
ATGGTTGTCGGGCTGGTGGCTCTGGGGATTTGGTCTGTCATGCAGCGCAATTACCTACAAGA  
TGAGAATGAAAATCGCACAGGAAGCTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG  
TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCCTGTGACACAAAC  
TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTAACATGGGAAGAGAG  
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG  
AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCGAAT  
GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGGGAAGA  
TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG  
AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT  
TAATGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT  
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA



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**FIGURE 306**

MQDEDEGYITLNIKTRKPALVSVGPASSSWWRVMALILLILCVGMVVGLVALGIWSVMQRNYL  
QDENENRTGTLQQ LAKRFCQYVVKQSELKGTFKGHKCSPCDTNWRYYG DSCYGF FRHNL TWE  
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMF EFL  
EDGKGNMNCAYFHNGKMHPTFCENKH YLMCERKAGMTKVDQLP

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**FIGURE 307**

CCCACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCTGCCAGTCTCGCCCCGCGATCCCGG  
CCCCGGGGCTGTGGCGTCGACTCCGACCCAGGCAGCCAGCAGCCCCGCGCGGGAGCCGGACCGC  
CGCCGGAGGAGCTCGGACGGCATGCTGAGCCCCCTCCTTTGCTGAAGCCCCGAGTGCGGAGAA  
GCCCCGGGCAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAG  
CGGAGGAGAAGGAGGAGGAGGCGAACCCAGAGAGGGGCAGCAAAGAAGCGGTGGTGGTGGG  
CGTCGTGGCCATGGCGGCGGCTATCGCCAGCTCGCTCATCCGTCAGAAGAGGCAAGCCCCGCG  
AGCGCGAGAAATCCAACGCCTGCAAGTGTGTCAGCAGCCCCAGCAAAGGCAAGACCAGCTGC  
GACAAAAACAAGTTAAATGTCTTTTCCCGGGTCAAACCTCTTCGGCTCCAAGAAGAGGCGCAG  
AAGAAGACCAGAGCCTCAGCTTAAGGGTATAGTTACCAAGCTATACAGCCGACAAGGCTACC  
ACTTGCACTGCAGGCGGATGGAACCATGATGGCACCAAAGATGAGGACAGCACTTACACT  
CTGTTTAACCTCATCCCTGTGGGTCTGCGAGTGGTGGCTATCCAAGGAGTTCAAACCAAGCT  
GTACTTGGAATGAACAGTGAGGGATACTTGTACACCTCGGAACTTTTACACCTGAGTGCA  
AATTCAAAGAATCAGTGTTTGAAAATTATTATGTGACATATTCATCAATGATATACCGTCAG  
CAGCAGTCAGGCCGAGGGTGGTATCTGGGTCTGAACAAAGAAGGAGAGATCATGAAAGGCAA  
CCATGTGAAGAAGAACAAGCCTGCAGCTCATTTTCTGCCTAAACCACTGAAAGTGGCCATGT  
ACAAGGAGCCATCACTGCACGATCTCACGGAGTTCTCCCGATCTGGAAGCGGGACCCCAACC  
AAGAGCAGAAGTGTCTCTGGCGTGCTGAACGGAGGCAAATCCATGAGCCACAATGAATCAAC  
GTAGCCAGTGAGGGCAAAGAAGGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAAT  
TCTTCTAGCAGTCCTTCACCCAAAAGTTCAAATTTGTCAGTGACATTTACCAAACAAACAGG  
CAGAGTTCACTATTCTATCTGCCATTAGACCTTCTTATCATCCATACTAAAGC

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**FIGURE 308**

></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA28498  
><subunit 1 of 1, 245 aa, 1 stop  
><MW: 27564, pI: 10.18, NX(S/T): 1  
MAAAIASSLIRQKRQAREREKSNACKCVSSPSKGKTSCKNKNLVFSRVKLFSGSKRRRRRP  
EPQLKGIVTKLYSRQGYHLQLQADGTIDGTDKEDSTYTFLNLI PVGLRVVAIQGVQTKLYLA  
MNSEGILYTSELFTECKFKESVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVK  
KNKPAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKSRSVSGVLNGGKSMHNEST

**N-glycosylation site.**

amino acids 242-246

**Glycosaminoglycan attachment site.**

amino acids 165-169, 218-222

**Tyrosine kinase phosphorylation site.**

amino acids 93-100

**N-myristoylation site.**

amino acids 87-93, 231-237

**ATP/GTP-binding site motif A (P-loop).**

amino acids 231-239

**HBGF/FGF family proteins**

amino acids 78-94, 102-153

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**FIGURE 309**

CCAGGATGGAGCTGGGGCCTGTATAGCCATATTATTGTTCTATGCTACTAGACATGGGGGGG  
ACTTGGTGAAAAAGGTATTATCCAGCCAGAGGGTCTGGGAGCCCTGTCTTACTGAACCTGGG  
CAACCTGGATATTCTGAGACATATTTTGGGGGGATTTCAGTGAAAAAGTGGGGGATCCCCCT  
CCATTTAGAGTGTAGCAAAGGAAAAACACCAAGGTTGGGTTCCCTCCTGACATTGGCAGTG  
CCCCAGTAGGGGTGGGATGAGCGAATATTCCCAAAGCTAAAGTCCCACACCCTGTAGATTAC  
AAGAGTGGATTTGGCAGGAGTGTGCCCCAAAATACAGTGGAAAGGTGCCTGAAGATATTTAA  
ACCACGTCTTGGAATTTAGTGGGTCTTGGCTTTGGGATAGGTGAAGTGAGGACAGACACTG  
GAGAGGAGGGAAAGGGGACGTTTTCAATAGGAGGCAAACTCGAGGGTGGGATCCACTGAGG  
AGTACATAGGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCCACGGGTGGTAACTGGCTGCT  
GTGGAGGGGGGTACGTGAGGGGGGGGTCTGGGGCTTATCCTCAGGTCCTGTGGGTGGGGCAG  
CGAGTCGGGGCCTGAGCGTCAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGGAGCCCAG  
CGCGCTCCGGGCGCCTGCCGGTTTGGGGGTGTCTCCTCCCGGGGCGCT**ATG**GCGGCGCTGGC  
CAGTAGCCTGATCCGGCAGAAGCGGGAGGTCCGCGAGCCCGGGGGCAGCCGGCCGGTGTCCG  
CGCAGCGGCGCGTGTGTCCCCGCGGCACCAAGTCCCTTTGCCAGAAGCAGCTCCTCATCCTG  
CTGTCCAAGGTGCGACTGTGCGGGGGGCGGCCCGCGCGGCCGACCGCGGCCCGGAGCCTCA  
GCTCAAAGGCATCGTCACCAAAGTGTCTGCCGCCAGGGTTTCTACCTCCAGGCGAATCCCC  
ACGGAAGCATCCAGGGCACCCCAGAGGATACCAGCTCCTTCACCCACTTCAACCTGATCCCT  
GTGGGCCTCCGTGTGGTCACCATCCAGAGCGCCAAGCTGGGTCACTACATGGCCATGAATGC  
TGAGGGACTGCTCTACAGTTCGCCGCATTTACAGCTGAGTGTGCTTTAAGGAGTGTGTCT  
TTGAGAATTACTACGTCTGTACGCCTCTGCTCTCTACCGCCAGCGTCGTTCTGGCCGGGCC  
TGGTACCTCGGCCTGGACAAGGAGGGCCAGGTCATGAAGGGAACCGAGTTAAGAAGACCAA  
GGCAGCTGCCCCACTTTCTGCCCAAGCTCCTGGAGGTGGCCATGTACCAGGAGCCTTCTCTCC  
ACAGTGTCCCCGAGGCCTCCCCCTCCAGTCCCCCTGCCCCC**TGAA**ATGTAGTCCCTGGACTG  
GAGGTTCCCTGCACTCCCAGTGAGCCAGCCACCACCACAACCTGT

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**FIGURE 310**

MAALASSLIRQKREVREPPGSRPVSAQRRVCPRGTKSLCQKQLLILLSKVRLCGGRPARPDR  
GPEPQLKGIVTKLFCRQGFYQLQANPDGSIQGTPEDTSSFTHFNLI PVGLRVVTIQSAKLGHY  
MAMNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNR  
VKKTKAAAHFLPKLLEVAMYQEPSLHSVPEASPSSPPAP

**Tyrosine kinase phosphorylation site:**

amino acids 199-207

**N-myristoylation sites:**

amino acids 54-60, 89-95, 131-137

**HBGF/FGF family signature:**

amino acids 131-155

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**FIGURE 311**

**ATG**GCCGCGGCCATCGCTAGCGGCTTGATCCGCCAGAAGCGGCAGGCGCGGGAGCAGCACTG  
GGACCGGCCGTCTGCCAGCAGGAGGCGGAGCAGCCCCAGCAAGAACCGCGGGCTCTGCAACG  
GCAACCTGGTGGATATCTTCTCCAAAGTGCGCATCTTCGGCCTCAAGAAGCGCAGGTTGCGG  
CGCCAAGATCCCCAGCTCAAGGGTATAGTGACCAGGTTATATTGCAGGCAAGGCTACTACTT  
GCAAATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCT  
TCAACCTCATAACAGTGGGACTACGTGTTGTTGCCATCCAGGGAGTGAAAACAGGTTGTAT  
ATAGCCATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTTACCCCTGAATGCAAGTT  
TAAAGAATCTGTTTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGG  
AATCTGGTAGAGCCTGGTTTTTGGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACAGA  
GTAAAGAAAACCAAACCAGCAGCTCATTTTCTACCCAAGCCATTGGAAGTTGCCATGTACCG  
AGAACCATCTTTGCATGATGTTGGGGAAACGGTCCCGAAGCCTGGGGTGACGCCAAGTAAAA  
GCACAAGTGCGTCTGCAATAATGAATGGAGGCAAACCAGTCAACAAGAGTAAGACAACA**TAG**

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**FIGURE 312**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA28503

&gt;&lt;subunit 1 of 1, 247 aa; 1 stop

&gt;&lt;MW: 27702, pI: 10.36, NX(S/T): 2

MAAAIASGLIRQKRQAREQHWDRPSASRRRSSPSKNRGLCNGNLVDIFSKVRI FGLKKRRLR  
RQDPQLKGIVTRLYCRQGYLQMHDPGALDGTKDDSTNSTLFNLI PVGLRVVAIQGVKTGLY  
IAMNGEGYLYPSELFTECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNR  
VKKTKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKSSTT

**N-glycosylation site.**

amino acids 100-104, 242-246

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 28-32, 29-33

**Tyrosine kinase phosphorylation site.**

amino acids 199-207

**N-myristoylation site.**

amino acids 38-44, 89-95, 118-124, 122-128, 222-228

**HBGF/FGF family proteins.**

amino acids 104-155, 171-198

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**FIGURE 313**

GGGGAGAGGAATTGACCATGTAAAAGGAGACTTTTTTTTTTGGTGGTGGTGGCTGTTGGGTGCCTTGCAAAAAT  
GAAGGATGCAGGACGCAGCTTTCTCCTGGAACCGAACGCAATGGATAAACTGATTGTGCAAGAGAGAAGGAAGA  
ACGAAGCTTTTTCTGTGAGCCCTGGATCTTAACACAAATGTGTATATGTGCACACAGGGAGCATTCAAGAATG  
AAATAAACAGAGTTAGACCCGCGGGGGTGGTGTGTTCTGACATAAATAAATAATCTTAAAGCAGCTGTTCCC  
CTCCCCACCCCCAAAAAAAGGATGATTGGAAATGAAGAACCGAGGATTCACAAAGAAAAAGTATGTTCAATTT  
TTCTCTATAAAGGAGAAAGTGAGCCAAGGAGATATTTTTGGAATGAAAAGTTTGGGGCTTTTTTAGTAAAGTAA  
AGAACTGGTGTGGTGGTGTTCCTTTCTTTTGAATTTCCCAAGAGGAGAGGAAATTAATAATACATCTGC  
AAAGAAATTTAGAGAGAAGAAAGTTGACCGCGGCAGATTGAGGCATTGATTGGGGGAGAGAAACAGCAGAGCA  
CAGTTGGATTTGTGCCTATGTTGACTAAAATTGACGGATAATTGCAGTTGGATTTTCTTCATCAACCTCCTTT  
TTTTTAAATTTTATTCTTTTGGTATCAAGATCATGCGTTTTCTCTTGTCTTAACCACTGGATTTCATCT  
GGATGTTGCTGTGATCAGTCTGAAATACAATGTTTGAATTCAGAAGGACCAACACCAGATAAATTATGAATG  
TTGAACAAGATGACCTTACATCCACAGCAGATAATGATAGGTCTAGGTTTAACAGGGCCCTATTTGACCCCT  
GCTTGTGGTGTGCTGGCTCTTCACTTCTTGTGGTGGCTGGTCTGGTGCAGGCTCAGACCTGCCCTTCTGTGT  
GCTCCTGCAGCAACCAGTTCAGCAAGGTGATTTGTGTTCCGAAAAACCTGCGTGAGGTTCCGGATGGCATCTCC  
ACCAACACACGGCTGCTGAACCTCCATGAGAACCAATCCAGATCATCAAAGTGAACAGCTTCAAGCACTTGAG  
GCACTTGGAATCCTACAGTTGAGTAGGAACCATATCAGAACCATTGAAATTGGGGCTTCAATGGTCTGGCGA  
ACCTCAACACTCTGGAACCTCTTGACAATCGTCTTACTACCATCCCGAATGGAGCTTTTGTATACTTGTCTAAA  
CTGAAGGAGCTCTGGTTGCGAAACAACCCATTGAAAGCATCCCTTCTTATGCTTTTAACAGAATTCTTCTTT  
GCGCCGACTAGACTTAGGGGAATTGAAAAGACTTTCATACATCTCAGAAGGTGCCTTTGAAGGTCTGTCCAAT  
TGAGGTATTTGAACCTTGCCATGTGCAACCTTCGGGAAATCCCTAACCTCACACCGCTCATAAACTAGATGAG  
CTGGATCTTTCTGGGAATCATTTATCTGCCATCAGGCCTGGCTCTTTCAGGGTTTGATGCACCTTCAAAAAT  
GTGGATGATACAGTCCCAGATTCAAGTGATTGAACGGAATGCCTTTGACAACCTTCAGTCACTAGTGGAGATCA  
ACCTGGCACACAATAATCTAACATTACTGCCTCATGACCTCTTCACTCCCTTGCATCATCTAGAGCGGATACAT  
TTACATCACAACCTTGGAAGTGTAACTGTGACATACTGTGGCTCAGCTGGTGGATAAAAGACATGGCCCCCTC  
GAACACAGCTTGTGTGCCCCGGTGTAACTCCTCCCAATCTAAAGGGGAGGTACATTGGAGAGCTCGACCAGA  
ATTACTTCACATGCTATGCTCCGGTGATTGTGGAGCCCCCTGCAGACCTCAATGTCACTGAAGGCATGGCAGCT  
GAGCTGAAATGTGGGCCTCCACATCCCTGACATCTGTATCTTGGATTACTCCAAATGGAACAGTCATGACACA  
TGGGGCGTACAAAGTGCGGATAGCTGTGCTCAGTGATGGTACGTTAAATTTACAAATGTAAGTGTGCAAGATA  
CAGGCATGTACACATGTATGGTGAGTAATCCGTTGGGAATACTACTGCTTCAGCCACCCTGAATGTTACTGCA  
GCAACCACTACTCCTTTCTTACTTTTCAACCGTCACAGTAGAGACTATGGAACCGTCTCAGGATGAGGCACG  
GACCACAGATAACAATGTGGGTCCCCTCCAGTGGTGCAGTGGGAGACCACCAATGTGACCACCTCTCTCACAC  
CACAGAGCACAAGGTCGACAGAGAAAACCTTCACCATCCCAGTGACTGATATAAACAGTGGGATCCCAGGAATT  
GATGAGGTCATGAAGACTACCAAAATCATCATTGGGTGTTTTGTGGCCATCACACTCATGGCTGCAGTGATGCT  
GGTCATTTTCTACAAGATGAGGAAGCAGCACCATCGGCAAAACCATCACGCCCCAACAAAGGACTGTTGAAATTA  
TTAATGTGGATGATGAGATTACGGGAGACACACCCATGGAAAGCCACCTGCCATGCCTGCTATCGAGCATGAG  
CACCTAAATCACTATAACTCATACAAATCTCCCTTCAACCACACAACAACAGTTAACACAATAAATTCAATACA  
CAGTTCAGTGCATGAACCGTTATTGATCCGAATGAACTCTAAAGACAATGTACAAGAGACTCAAATCTAAACA  
TTTACAGAGTTACAAAAACAAACAATCAAAAAAAGACAGTTTATTAAAAATGACACAAATGACTGGGCTAA  
ATCTACTGTTTCAAAAAAGTGTCTTTACAAAAAACAAGAAAGAAATTTATTTATTAATAATCTATTG  
TGATCTAAAGCAGACAAAAA



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**FIGURE 314**

MLNKMTLHPQQIMIGPRFNRALFDPLLVLALLQLLVVAGLVRAQTCPSCVSCSNQFSKVIC  
VRKNLREVPDGI STNTRLLNLHENQIQIIKVNSFKHLRHLEILQLSRNHIRTIEIGAFNGLA  
NLNTLELFDNRLTTIPNGAFVYLSKLKELWLRNPNPIESIPSYAFNRIPSLRRLDLGELKRLS  
YISEGAFEGLSNLRYNLAMCNLREIPNLTPLIKLDELDSLGNHLSAIRPGSFQGLMHLQKL  
WMIQSQIQVIERNAFDNLQSLVEINLAHNNLTLLPHDLFTPLHHLERIHLLHNPWNCNDIL  
WLSWWIKDMAPSNTACCARCNTPPNLKGRYIGELDQNYFTCYAPVIVEPPADLNVTEGMAAE  
LKCRASSTLSVSWITPNGTVMTHGAYKVRIAVLSDGTLNFTNVTQDTGMYTCMVSNSVGN  
TTASATLNVTAATTTTFSYFSTVTVETMEPSQDEARTTDNNVGPTPVVDWETTNVTTSLTPQ  
STRSTEKTFTIPVTDINSGIPGIDEVMKTTKIIIGCFVAITLMAAVMLVIFYKMRKQHRQN  
HHAPTRTVEIINVDDEITGDTPMESHLPMPAIEHEHLNHYNSYKSPFNHTTTVNTINSIHSS  
VHEPLLIRMNSKDNVQETQI

**Signal sequence:**

amino acids 1-44

**Transmembrane domain:**

amino acids 523-543

**N-glycosylation site.**amino acids 278-282, 364-368, 390-394, 412-416, 415-419,  
434-438, 442-446, 488-492, 606-610**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 183-187

**Casein kinase II phosphorylation site.**

amino acids 268-272, 417-421, 465-469, 579-583, 620-624

**N-myristoylation site.**amino acids 40-46, 73-79, 118-124, 191-197, 228-234, 237-243,  
391-397, 422-428, 433-439, 531-537

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**FIGURE 315**

GCGCCGGGAGCCCATCTGCCCCAGGGGCACGGGGCGCGGGGCCGGCTCCCGCCCGGCACAT  
GGCTGCAGCCACCTCGCGCGCACCCCGAGGCGCCGCGCCAGCTCGCCCGAGGTCCGTCCGA  
GGCGCCCGGGCCCGCCCGGAGCCAAGCAGCAACTGAGCGGGGAAGCGCCCGCGTCCGGGGATC  
GGG**ATG**TCCCTCCTCCTTCTCCTCTTGCTAGTTTCTACTATGTTGGAACCTTGGGGACTCA  
CACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACCTTGCCCTGCCACCATCAACTGGGGC  
TTCCAGAAAAAGACACTCTGGATATTGAATGGCTGCTCACCGATAATGAAGGGAACCAAAAA  
GTGGTGATCACTTACTCCAGTCGTCATGTCTACAATAACTTGACTGAGGAACAGAAGGGCCG  
AGTGGCCTTTGCTTCCAATTTCTGGCAGGAGATGCCTCCTTGAGATTGAACCTCTGAAGC  
CCAGTGATGAGGGCCGGTACACCTGTAAGGTTAAGAATTCAGGGCGCTACGTGTGGAGCCAT  
GTCATCTTAAAAGTCTTAGTGAGACCATCCAAGCCCAAGTGTGAGTTGGAAGGAGAGCTGAC  
AGAAGGAAGTGACCTGACTTTGCAGTGTGAGTCATCCTCTGGCACAGAGCCCATTGTGTATT  
ACTGGCAGCGAATCCGAGAGAAAGAGGGAGAGGATGAACGTCTGCCTCCCAAATCTAGGATT  
GACTACAACCACCCTGGACGAGTTCTGCTGCAGAATCTTACCATGTCTACTCTGGACTGTA  
CCAGTGCACAGCAGGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCGAGTAAGTGTACAGT  
ATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTG  
ATTTTCCTCTTGTTGTGGCTGCTAATCCGAAGGAAAGACAAAGAAAGATATGAGGAAGAAGA  
GAGACCTAATGAAATTCGAGAAGATGCTGAAGCTCCAAAAGCCCGTCTTGTGAAACCCAGCT  
CCTCTTCCTCAGGCTCTCGGAGCTCACGCTCTGGTTCTTCCTCCACTCGCTCCACAGCAAAT  
AGTGCCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGGCCAC  
CCAGGCATACAGCCTAGTGGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATG  
CTAATCTGACCAAAGCAGAAACCACCCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAA  
ACGGTCT**TGA**ATTACAATGGACTTGACTCCACGCTTTCTTAGGAGTCAGGGTCTTTGGACTC  
TTCTCGTCATTGGAGCTCAAGTCACCAGCCACACAACCAGATGAGAGGTCATCTAAGTAGCA  
GTGAGCATTGCACGGAACAGATTCAGATGAGCATTTCCTTATACAATACCAAACAAGCAAA  
AGGATGTAAGCTGATTCATCTGTAAAAGGCATCTTATTGTGCCTTTAGACCAGAGTAAGGG  
AAAGCAGGAGTCCAAATCTATTTGTTGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTG  
AGGTGAATATACCTAAACTTTTAATGTGGGATATTTTGTATCAGTGCTTTGATTCACAATT  
TTCAAGAGGAAATGGGATGCTGTTGTAAATTTCTATGCATTTCTGCAAACTTATTGGATT  
ATTAGTTATTACAGACAGTCAAGCAGAACCCACAGCCTTATTACACCTGTCTACACCATGTAC  
TGAGCTAACCACCTCTAAGAACTCCAAAAAGGAAACATGTGTCTTCTATTCTGACTTAAC  
TTCATTTGTCATAAGGTTTGGATATTAATTTCAAGGGGAGTTGAAATAGTGGGAGATGGAGA  
AGAGTGAATGAGTTTCTCCCACTCTATACTAATCTCACTATTTGTATTGAGCCCCAAAATAAC  
TATGAAAGGAGACAAAAATTTGTGACAAAGGATTGTGAAGAGCTTTCCATCTTCATGATGTT  
ATGAGGATTGTTGACAAACATTAGAAATATATAATGGAGCAATTGTGGATTTCCCTCAAAT  
CAGATGCCTCTAAGGACTTTCTGCTAGATATTTCTGGAAGGAGAAAATACAACATGTCATT  
TATCAACGTCCTTAGAAAGAATTCTTCTAGAGAAAAAGGGATCTAGGAATGCTGAAAGATTA  
CCCAACATACCATTATAGTCTCTTCTTTCTGAGAAAATGTGAAACCAGAATTGCAAGACTGG  
GTGGACTAGAAAGGGAGATTAGATCAGTTTTCTCTTAATATGTCAAGGAAGGTAGCCGGGCA  
TGGTGCCAGGCACCTGTAGGAAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCC  
ATTGCACTCCAGCCTGGGTGACAGAGCGGGACTCCGTCTC —

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**FIGURE 316**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45419

&gt;&lt;subunit 1 of 1, 373 aa, 1 stop

&gt;&lt;MW: 41281, pI: 8.33, NX(S/T): 3

MSLLLLLLLLVSYYVGTLGTHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKV  
VITYSSRHVYNNLTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHV  
ILKVLVRPSKPKCELEGELTEGSDTLQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRID  
YNHPGRVLLQNLTMSYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLI  
FLLVWLLIRRDKERYEEEEERPNEIREDAEAPKARLVKPSSSSSGSRSSRSGSSSTRSTANS  
ASRSQRTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHANLTKAETTPSMIPSQSRAFQTV

**Signal sequence:**

amino acids 1-16

**Transmembrane domain:**

amino acids 232-251

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**FIGURE 317**

CGCGAGGCGCGGGGAGCCTGGGACCAGGAGCGAGAGCCGCCTACCTGCAGCCGCCGCCACGGCACGGCAGCCCA  
CCATGGCGCTCCTGCTGTGCTTCGTGCTCCTGTGCGGAGTAGTGGATTTGCCAGAAAGTTGAGTATCACTACT  
CCTGAAGAGATGATTGAAAAAGCCAAAGGGGAAACTGCCTATCTGCCATGCAAATTTACGCTTAGTCCCGAAGA  
CCAGGGACCGCTGGACATCGAGTGGCTGATATCACCAGCTGATAATCAGAAGGTGGATCAAGTGATTATTTTAT  
ATTCTGGAGACAAAATTTATGATGACTACTATCCAGATCTGAAAGGCCGAGTACATTTTACGAGTAATGATCTC  
AAATCTGGTGATGCATCAATAAATGTAACGAATTTACAACGTGCAGATATTGGCACATATCAGTGCAAAGTGAA  
AAAAGCTCCTGGTGTGCAAATAAGAAGATTCATCTGGTAGTTCTTGTAAAGCCTTCAGTGCGAGATGTTACG  
TTGATGGATCTGAAGAAATTGGAAGTGACTTTAAGATAAAATGTGAACCAAAGAAGGTTCACTTCCATTACAG  
TATGAGTGGCAAAAATGTCTGACTCACAGAAAATGCCCACTTCATGGTTAGCAGAAATGACTTCATCTGTTAT  
ATCTGTAAAAATGCCTCTTCTGAGTACTCTGGGACATACAGCTGTACAGTCAGAAACAGAGTGGGCTCTGATC  
AGTGCCTGTTGCGCTCAAACGTTGTCCCTCCTTCAAATAAAGCTGGACTAATTGCAGGAGCCATTATAGGAAC  
TTGCTTGCTCTAGCGCTCATTGGTCTTATCATCTTTTGCTGTGCTGTAAGCGCAGAGAAGAAAAATATGAAA  
GGAAGTTCATCAGATATCAGGGAAGATGTGCCACCTCCAAAGAGCCGTACGTCCACTGCCAGAAGCTACATCG  
GCAGTAATCATTCATCCCTGGGGTCCATGTCTCCTTCCAACATGGAAGGATATTCCAAGACTCAGTATAACCAA  
GTACCAAGTGAAGACTTTGAACGCACTCCTCAGAGTCCGACTCTCCACCTGCTAAGTTCAAGTACCCTTACAA  
GACTGATGGAATTACAGTTGTATTAATATGGACTACTGAAGAATCTGAAGTATTGTATTATTTGACTTTATTTT  
AGGCCTCTAGTAAAGACTTAAATGTTTTTAAAAAAGCACAAAGGCACAGAGATTAGAGCAGCTGTAAGAACAC  
ATCTACTTTATGCAATGGCATTAGACATGTAAGTCAGATGTATGTCAAATTAGTACGAGCCAAATTCCTTGT  
TAAAAAACCTATGTATAGTGACACTGATAGTTAAAAGATGTTTTATTATATTTTCAATAACTACCACTAACAA  
ATTTTTAACTTTTCATATGCATATTCGATATGTGGTCTTTTAGGAAAAGTATGGTTAATAGTTGATTTTTCAA  
AGGAAATTTTTAAATTTCTTACGTTCTGTTTAAATGTTTTTGCTATTTAGTTAAATACATTGAAGGAAATACCCG  
TTCTTTTCCCCTTTTATGCACACAACAGAAAACGCGTTGTCTCATGCTCAAACATTTTTTTATTTGCAACTACA  
TGATTTACACAATTTCTCTTAAACAACGACATAAAATAGATTTCTTGTATATAAATAACTTACATACGCTCCA  
TAAAGTAAATTTCTCAAAGGTGCTAGAACAAATCGTCCACTTCTACAGTGTTCTCGTATCCAACAGAGTTGATGC  
ACAATATATAAATACTCAAGTCCAATATTA AAAA ACTTAGGCACTTGACTAACTTTAATAAAATTTCTCAAAC  
TATCAATATCTAAAGTGCATATATTTTTTAAGAAAGATTATTTCTCAATAACTTCTATAAAAAATAAGTTTGATGG  
TTTGGCCCATCTAACTTCACTACTATTAGTAAGAATTTTAACTTTTAAATGTGTAGTAAGGTTTATTCTACCTT  
TTTCTCAACATGACACCAACACAATCAAAAACGAAGTTAGTGAGGTGCTAACATGTGAGGATTAATCCAGTGAT  
TCCGGTCACAAATGCATTCCAGGAGGAGGTACCCATGTCACTGGAATTGGGCGATATGGTTTATTTTTTCTTCCC  
TGATTTGGATAACCAATGGAACAGGAGGAGGATAGTGATTCTGATGGCCATTCCCTCGATACATTCCCTGGCTT  
TTTTCTGGGCAAAGGTTGCCACATTGGAAGAGGTGGAATATAAGTTCTGAAATCTGTAGGGAAGAGAACACAT  
TAAGTTAATTCAAAGGAAAAAATCATCTATGTTCCAGATTTCTCATTAAAGACAAAGTTACCCACAACACT  
GAGATCACATCTAAGTGACACTCCTATTGTGAGGTCTAAATACATTAAAAACCTCATGTGTAATAGGCGTATAA  
TGTATAACAGGTGACCAATGTTTTCTGAATGCATAAAGAAATGAATAAACTCAAACACAGTACTTCCATAAACAA  
CTTCAACCAAAAAAGACCAAAACATGGAACGAATGGAAGCTTGTAAGGACATGCTTGTTTTAGTCCAGTGGTTT  
CCACAGCTGGCTAAGCCAGGAGTCACTTGGAGGCTTTTAAATACAAAACATTGGAGCTGGAGGCCATTATCCTT  
AGCAAATAATGCAGAAACAGAAATCAACTACCGCATGTTCTCACTTATAAGTGGGAGGTAATGATAAGAACT  
TATGAACACAAAGAAGGAAACAATAGACATTGGAGTCTATTTGAGAGGGGAGGGTGGGAGAAGGAAAGGAGCA  
GAAAAGATAACTATTGAGTACTGCCTTCACACCTGGGTGATGAAATAATATGTACAACAAATCCCTGTGACACA  
TGTTTACCTATGGAACAAACCTTCATGTGTATCCCTAAACCTAAAAATAAAAGTTAAAAAARAAAAA  
AAAAA

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**FIGURE 318**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA82361

&gt;&lt;subunit 1 of 1, 352 aa, 1 stop

&gt;&lt;MW: 38938, pI: 7.86, NX(S/T): 3

MALLLCFVLLCGVVDFARSLSITTPPEEMIEKAKGETAYLPCKFTLSPEDQGPLDIEWLISPA  
DNQKVDQVIILYSGDKIYDDYYPDLKGRVHFTSNDLKSGDASINVTNLQLSDIGTYQCKVKK  
APGVANKKIHLVVLVKPSGARCIVDGSEEIGSDFKIKCEPKESLPLQYEWQKLSDSQKMPT  
SWLAEMTSSVISVKNASSEYSGTYSCTVRNRVGSQCLLRNLNVPPSPNKAGLIAGAIIGTLL  
ALALIGLIIFCCRKKRREEKYEKEVHHDIREDVPPPKSRTSTARSYIGSNHSSLGSMSPSNM  
EGYSKTQYNQVPSEDFERTPQSPTLPPAKFKYPYKTDGITVV

**Signal sequence.**

amino acids 1-19

**Transmembrane domain:**

amino acids 236-257

**N-glycosylation sites.**

amino acids 106-110, 201-205, 298-302

**Tyrosine kinase phosphorylation sites.**

amino acids 31-39, 78-85, 262-270

**N-myristoylation sites.**amino acids 116-122, 208-214, 219-225, 237-243, 241-247,  
245-251, 296-302**Myelin P0 protein.**

amino acids 96-125

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**FIGURE 319**

TGAAATGACTTCCACGGCTGGGACGGGAACCTTCCACCCACAGCTATGCCTCTGATTGGTGA  
ATGGTGAAGGTGCCTGTCTAACTTTTCTGTAAAAAGAACCAGCTGCCTCCAGGCAGCCAGCC  
CTCAAGCATCACTTACAGGACCAGAGGGACAAGACATGACTGTGATGAGGAGCTGCTTTCGC  
CAATTTAACACCAAGAAGAATTGAGGCTGCTTGGGAGGAAGGCCAGGAGGAACACGAGACTG  
AGAGATGAATTTTCAACAGAGGCTGCAAAGCCTGTGGACTTTAGCCAGACCCTTCTGCCCTC  
CTTTGCTGGCGACAGCCTCTCAAATGCAGATGGTTGTGCTCCCTTGCTGGGTTTTACCCTG  
CTTCTCTGGAGCCAGGTATCAGGGGCCAGGGCCAAGAATTCCACTTTGGGCCCTGCCAAGT  
GAAGGGGGTTGTTCCCCAGAACTGTGGGAAGCCTTCTGGGCTGTGAAAGACACTATGCAAG  
CTCAGGATAACATCACGAGTGCCCGGCTGCTGCAGCAGGAGGTTCTGCAGAACGTCTCGGAT  
GCTGAGAGCTGTTACCTTGTCCACACCCTGCTGGAGTTCTACTTGAAAACGTTTTTCAAAAA  
CCACCACAATAGAACAGTTGAAGTCAGGACTCTGAAGTCATTCTCTACTCTGGCCAACAAC  
TTGTTCTCATCGTGTCACTGCAACTGCAACCCAGTCAAGAAAAATGAGATGTTTTCCATCAGAGAC  
AGTGACACACAGGCGGTTTTCTGCTATTCCGGAGAGCATTCAAACAGTTGGACGTAGAAGCAGC  
TCTGACCAAAGCCCTTGGGGAAGTGGACATTCTTCTGACCTGGATGCAGAAATTCTACAAGC  
TCTTGAATGTCTAGACCAGGACCTCCCTCCCCCTGGCACTGGTTTTGTTCCCTGTGTCAATTTCA  
AACAGTCTCCCTTCCCTATGCTGTTCACTGGACACTTCACGCCCTTGGCCATGGGTCCCATTCT  
TTGGCCCAGGATTATTGTCAAAGAAGTCATTCTTTAAGCAGCGCCAGTGACAGTCAGGGGAAG  
GTGCCTCTGGATGCTGTGAAGAGTCTACAGAGAAGATTCTTGATTTTATTACAACCTCTATTT  
AATTAATGTCAGTATTTCAACTGAAGTTCTATTTATTTGTGAGACTGTAAGTTACATGAAGG  
CAGCAGAAATATTGTGCCCCATGCTTCTTTACCCCTCACAATCCTTGCCACAGTGTGGGGCAG  
TGGATGGGTGCTTAGTAAGTACTTAATAAACTGTGGTGCTTTTTTTGGCCTGTCTTTGGATT  
GTTAAAAAACAGAGAGGGATGCTTGGATGTAAAACTGAACTTCAGAGCATGAAAATCACACT  
GTCTTCTGATATCTGCAGGGACAGAGCATTGGGGTGGGGGTAAAGGTGCATCTGTTTGAAAAG  
TAAACGATAAAATGTGGATTAAAGTGCCAGCACAAAGCAGATCCTCAATAAACATTTTCATT  
TCCCACCCACACTCGCCAGCTCACCCCATCATCCCTTTCCCTTGGTGCCCTCCTTTTTTTTTT  
TATCCTAGTCATTCTTCCCTAATCTTCCACTTGAGTGTCAAGCTGACCTTGCTGATGGTGAC  
ATTGCACCTGGATGTACTATCCAATCTGTGATGACATTCCCTGCTAATAAAAGACAACATAA  
CTCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 320**

&gt;&lt;/usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA88002

&gt;&lt;subunit 1 of 1, 206 aa, 1 stop

&gt;&lt;MW: 23799, pI: 9.12, NX(S/T): 3

MNFQQRLQSLWTLARPFPCPLLATASQMOMVVLPCLGFTLLLWSQVSGAQGQEFHFGPCQVK  
GVVPQKLWEAFWAVKDTMQAQDNITSARLLQQEVLQNVSDAESCYLEVHTLLEFYLKTVFKNH  
HNRTVEVRTLKSFSTLANNFVLIVSQLQPSQENEMFSIRDSAHRRFLLFRRAFKQLDVEAAL  
TKALGEVDILLTWMQKFYKL

**Signal sequence:**

amino acids 1-42

**N-glycosylation sites.**

amino acids 85-89, 99-103, 126-130

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**FIGURE 321**

AAGGAGCAGCCCGCAAGCACCAAGTGAGAGGCATGAAGTTACAGTGTGTTTCCCTTTGGCTC  
CTGGGTACAATACTGATATTGTGCTCAGTAGACAACCACGGTCTCAGGAGATGTCTGATTTT  
CACAGACATGCACCATATAGAAGAGAGTTTCCAAGAAATCAAAGAGCCATCCAAGCTAAGG  
ACACCTTCCCAAATGTCACTATCCTGTCCACATTGGAGACTCTGCAGATCATTAAAGCCCTTA  
GATGTGTGCTGCGTGACCAAGAACCTCCTGGCGTTCTACGTGGACAGGGTGTTCAAGGATCA  
TCAGGAGCCAAACCCCAAAATCTTGAGAAAAATCAGCAGCATTGCCAACTCTTTCCTCTACA  
TGCAGAAAACCTCTGCGGCAATGTCAGGAACAGAGGCAGTGTCACTGCAGGCAGGAAGCCACC  
AATGCCACCAGAGTCATCCATGACAACTATGATCAGCTGGAGGTCCACGCTGCTGCCATTAA  
ATCCCTGGGAGAGCTCGACGTCTTTCTAGCCTGGATTAATAAGAATCATGAAGTAATGTTCT  
CAGCTTGATGACAAGGAACCTGTATAGTGATCCAGGGATGAACACCCCCTGTGCGGTTTACT  
GTGGGAGACAGCCCACCTTGAAGGGGAAGGAGATGGGGAAGGCCCTTGCAGCTGAAAGTCC  
CACTGGCTGGCCTCAGGCTGTCTTATTCCGCTTGAAAATAGGCAAAAAGTCTACTGTGGTAT  
TTGTAATAAACTCTATCTGCTGAAAGGGCCTGCAGGCCATCCTGGGAGTAAAGGGCTGCCTT  
CCCATCTAATTTATTGTAAAGTCATATAGTCCATGTCTGTGATGTGAGCCAAGTGATATCCT  
GTAGTACACATTGTACTGAGTGGTTTTTCTGAATAAATTCCATATTTTACCTATGA



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**FIGURE 322**

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92282
><subunit 1 of 1, 177 aa, 1 stop
><MW: 20452, pI: 8.00, NX(S/T): 2
MKLQCVSLWLLGTILILCSVDNHGLRRCLISTDMHHIEESFQEIKRAIQAKDTFPNVTILST
LETLQIIKPLDVCCVTKNLLAFYVDRVFKDHQEPNPKILRKISSIANSFLYMQKTLRQCQEQ
RQCHCRQEATNATRVIHNDYDQLEVHAAAIKSLGELDVFLAWINKNHEVMFSA
```

**Signal sequence:**

amino acids 1-18

**N-glycosylation sites.**

amino acids 56-60, 135-139

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 102-106

**N-myristoylation site.**

amino acids 24-30

**Actinin-type actin-binding domain signature 1.**

amino acids 159-169

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**FIGURE 323**

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACTTGGCTTCGTTAG  
AACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTTAGGTGACACTAT  
AGAATAACATCCACTTTGCCTTTCTCTCCACAGGTGTCCACTCCCAGGTCCAACGACCTC  
GGTTCTATCGATAATCTCAGCACCAGCCACTCAGAGCAGGGCACGATGTTGGGGGCCCCGCCT  
CAGGCTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCATGAGCGTCCTCAGAGCCTATCCCA  
ATGCCTCCCCACTGCTCGGCTCCAGCTGGGGTGGCCTGATCCACCTGTACACAGCCACAGCC  
AGGAACAGCTACCACCTGCAGATCCACAAGAATGGCCATGTGGATGGCGCACCCCATCAGAC  
CATCTACAGTGCCCTGATGATCAGATCAGAGGATGCTGGCTTTGTGGTGATTACAGGTGTGA  
TGAGCAGAAGATACCTCTGCATGGATTTTCAGAGGCAACATTTTTGGATCACACTATTTTCGAC  
CCGGAGAACTGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCC  
TCAGTATCACTTCCTGGTCAGTCTGGGCCGGGCGAAGAGAGCCTTCCTGCCAGGCATGAACC  
CACCCCCGTA CTCCCAGTTCTGTCCCGGAGGAACGAGATCCCCCTAATTCACTTCAACACC  
CCCATAACACGGCGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCTGAACGT  
GCTGAAGCCCCGGGCCCCGGATGACCCCGGCCCGGCCTCCTGTTTACAGGAGCTCCCGAGCG  
CCGAGGACAACAGCCCGATGGCCAGTGACCCATTAGGGGTGGTCAGGGGCGGTTCGAGTGAAC  
ACGCACGCTGGGGGAACGGGCCCCGAAGGCTGCCGCCCTTCGCCAAGTTCATCTAGGGTCG  
CTGG

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**FIGURE 324**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA142238  
><subunit 1 of 1, 251 aa, 1 stop  
><MW: 27954, pI: 9.22, NX(S/T): 1  
MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSWGGLIHLYTATARNSYHLQIHKNGHVD  
GAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTLNGY  
DVIHSPQYHFLVSLGRAKRAFLPGMNPPPYSQLSRNEIPLIHFNTPIPRRHTRSAEDDSE  
RDPLNVLKPRARMTAPASCSQELPSAEDNSPMASDPLGVVRGGRVNT HAGGTGPEGCRPFA  
KFI

**Important features of the protein:**

**Signal peptide:**

amino acids 1-24

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 175-179

**N-myristoylation site.**

amino acids 33-39, 100-106, 225-231, 229-235

**HBGF/FGF family proteins**

amino acids 73-124

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**FIGURE 325**

GGAAAAGGTACCCGCGAGAGACAGCCAGCAGTTCTGTGGAGCAGCGGTGGCCGGCTAGG**ATG**  
GGCTGTCTCTGGGGTCTGGCTCTGCCCCCTTTCTTCTTCTGCTGGGAGGTTGGGGTCTCTGG  
GAGCTCTGCAGGCCCCAGCACCCGCGAGAGCAGACACTGCGATGACAACGGACGACACAGAAG  
TGCCCGCTATGACTCTAGCACCGGGCCACGCCGCTCTGGAAACTCAAACGCTGAGCGCTGAG  
ACCTCTTCTAGGGCCTCAACCCCAGCCGGCCCCATTCCAGAAGCAGAGACCAGGGGAGCCAA  
GAGAATTTCCCCCTGCAAGAGAGACCAGGAGTTTCACAAAACATCTCCCAACTTCATGGTG  
TGATCGCCACCTCCGTGGAGACATCAGCCGCCAGTGGCAGCCCCGAGGGAGCTGGAATGACC  
ACAGTTCAGACCATCACAGGCAGTGATCCCGAGGAAGCCATCTTTGACACCCTTTGCACCGA  
TGACAGCTCTGAAGAGGCAAAGACACTCACAATGGACATATTGACATTGGCTCACACCTCCA  
CAGAAGCTAAGGGCCTGTCCTCAGAGAGCAGTGCCTCTTCCGACGGCCCCCATCCAGTCATC  
ACCCCGTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCC  
GTCACGGGCCTCAGAGAGCAGCGCCTCTTCCGACGGCCCCCATCCAGTCATCACCCCGTCAT  
GGTCCCCGGGATCTGATGTCACTCTCCTCGCTGAAGCCCTGGTGACTGTCACAAACATCGAG  
GTTATTAATTGCAGCATCACAGAAATAGAAACAACAACTTCCAGCATCCCTGGGGCCTCAGA  
CATAGATCTCATCCCCACGGAAGGGGTGAAGGCCTCGTCCACCTCCGATCCACCAGCTCTGC  
CTGACTCCACTGAAGCAAAACCACACATCACTGAGGTACAGCCTCTGCCGAGACCCTGTCC  
ACAGCCGGCACCACAGAGTCAGCTGCACCTCATGCCACGGTTGGGACCCCACTCCCCACTAA  
CAGCGCCACAGAAAGAGAAGTGACAGCACCCGGGGCCACGACCCTCAGTGGAGCTCTGGTCA  
CAGTTAGCAGGAATCCCCTGGAAGAAACCTCAGCCCTCTCTGTTGAGACACCAAGTTACGTC  
AAAGTCTCAGGAGCAGCTCCGGTCTCCATAGAGGCTGGGTGAGCAGTGGGCAAAACAACCTC  
CTTTGCTGGGAGCTCTGCTTCCTCCTACAGCCCCTCGGAAGCCGCCCTCAAGAACTTCACCC  
CTTCAGAGACACCGACCATGGACATCGCAACCAAGGGGCCCTTCCCCACCAGCAGGGACCCT  
CTTCCTTCTGTCCCTCCGACTACAACCAACAGCAGCCGAGGGACGAACAGCACCTTAGCCAA  
GATCACAACCTCAGCGAAGACCACGATGAAGCCCCAACAGCCACGCCCACGACTGCCCCGGAC  
GAGGCCGACCACAGACG**TG**AGTGCAGGTGAAAATGGAGGTTTCCTCCTCCTGCGGCTGAGTG  
TGGCTTCCCCGGAAGACCTCACTGACCCCAGAGTGGCAGAAAGGCTGATGCAGCAGCTCCAC  
CGGGAACCTCACGCCCACGCGCCTCACTTCCAGGTCTCCTTACTGCGTGTCAGGAGAGGCTA  
ACGGACATCAGCTGCAGCCAGGCATGTCCCGTATGCCAAAAGAGGGTGCTGCCCCCTAGCCTG  
GGCCCCCACCAGACAGACTGCAGCTGCGTTACTGTGCTGAGAGGTACCCAGAAGGTTCCCATG  
AAGGGCAGCATGTCCAAGCCCCTAACCCCAGATGTGGCAACAGGACCCTCGCTCACATCCAC  
CGGAGTGTATGTATGGGGAGGGGCTTACCTGTTCCAGAGGTGTCCTTGGACTCACCTTGG  
CACATGTTCTGTGTTTCAGTAAAGAGAGACCTGATCACCCATCTGTGTGCTTCCATCCTGCA  
TTAAATTTCACTCAGTGTGGCCCCAAAAAAA

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**FIGURE 326**

MGCLWGLALPLFFFCWEVGVSGSSAGPSTRRADTAMTTDDTEVPAMTLAPGHAALETQTL  
ETSSRASTPAGPIPEAETRGAKRISPAETRSFTKTSPNFMVLIATSVETSAASGSPEGAGM  
TTVQITITGSDPEEAI FDTLCTDDSS EEAKTLTMDILTLAHTSTEAKGLSSESSASSDGPHPV  
ITPSRASESSASSDGPHPVITPSRASESSASSDGPHPVITPSWSPGSDVTLLAEALVTVTNI  
EVINCSITEIETTTSSIPGASDIDLIPTEGVKASSTSDPPALPDSTEAKPHITEVTASAETL  
STAGTTESAAPHATVGTPLPTNSATEREVTAPGATTLGALVTVSRNPLEETSALS VETPSY  
VKVSGAAPVSIEAGSAVGKTTSFAGSSASSYSPSEAALKNFTPSETPTMDIATKGPFPTSRD  
PLPSVPPTTTNSSRGTNSTLAKITTSAKTTMKPQQPRPRLPGRGRPQT

**N-glycosylation sites:**

amino acids 252-256, 445-449, 451-455

**cAMP-and cGMP-dependent protein kinase phosphorylation site.**

amino acids 84-90

**Casein kinase II phosphorylation sites.**amino acids 37-41, 108-112, 131-135, 133-137, 148-152, 165-169,  
246-250, 254-258, 256-260, 269-273, 283-287, 333-337, 335-339,  
404-408, 414-418, 431-435**N-myristoylation sites.**amino acids 2-8, 19-25, 117-123, 121-127, 232-238, 278-284, 314-  
320, 349-355, 386-392, 397-403, 449-455**ATP/GTP-binding site motif A (P-loop).**

amino acids 385-393

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**FIGURE 327**

GCGGAGCATCCGCTGCGGTCCTCGCCGAGACCCCCGCGCGGATTGCGCCGGTCCTTCCCGCGG  
GCGCGACAGAGCTGTCCTCGCACCTGGATGGCAGCAGGGGCGCCGGGGTCCTCTCGACGCCA  
GAGAGAAATCTCATCATCTGTGCAGCCTTCTTAAAGCAAACCTAAGACCAGAGGGAGGATTAT  
CCTTGACCTTTGAAGACCAAACTAACTGAAATTTAAATGTTCTTCGGGGGAGAAGGGAG  
CTTGACTTACACTTTGGTAATAATTTGCTTCCTGACACTAAGGCTGTCTGCTAGTCAGAATT  
GCCTCAAAAAGAGTCTAGAAGATGTTGTGTCATTGACATCCAGTCATCTCTTTCTAAGGGAATC  
AGAGGCAATGAGCCCGTATATACTTCAACTCAAGAAGACTGCATTAATTCTTGCTGTTCAAC  
AAAAACATATCAGGGGACAAAGCATGTAACCTGATGATCTTCGACACTCGAAAAACAGCTA  
GACAACCCAACTGCTACCTATTTTTCTGTCCCAACGAGGAAGCCTGTCCATTGAAACCAGCA  
AAAGGACTTATGAGTTACAGGATAATTACAGATTTTCCATCTTTGACCAGAAATTTGCCAAG  
CCAAGAGTTACCCAGGAAGATTCTCTCTTACATGGCCAATTTTCAAGCAGTCACTCCCC  
TAGCCCATCATCACACAGATTATTCAAAGCCCACCGATATCTCATGGAGAGACACACTTTCT  
CAGAAGTTTGGATCCTCAGATCACCTGGAGAACTATTTAAGATGGATGAAGCAAGTGCCCA  
GCTCCTTGCTTATAAGGAAAAAGGCCATTCTCAGAGTTCACAATTTTCTCTGATCAAGAAA  
TAGTCTCATCTGCTGCCTGAAAATGTGAGTGCGCTCCAGCTACGGTGGCAGTTGCTTCTCCA  
CATACCACCTCGGCTACTCCAAAGCCCGCCACCCTTCTACCCACCAATGCTTCAGTGACACC  
TTCTGGGACTTCCCAGCCACAGCTGGCCACCACAGCTCCACCTGTAACCACTGTCACTTCTC  
AGCTCCCACGACCCTCATTTCTACAGTTTTTACACGGGCTGCGGCTACACTCCAAGCAATG  
GCTACAACAGCAGTTCTGACTACCACCTTTCAGGCACCTACGGACTCGAAAGGCAGCTTAGA  
AACCATACCGTTTACAGAAATCTCCAACCTAACTTTGAACACAGGGAATGTGTATAACCCTA  
CTGCACTTTCTATGTCAAATGTGGAGTCTTCCACTATGAATAAACTGCTTCCTGGGAAGGT  
AGGGAGGCCAGTCCAGGCAGTTCCTCCAGGGCAGTGTTCCAGAAAATCAGTACGGCCTTCC  
ATTTGAAAAATGGCTTCTTATCGGGTCCCTGCTCTTTGGTGTCTGTTCTGCTGGTGATAGGCC  
TCGTCTCTCTGGGTAGAATCCTTTCGGAATCACTCCGCAGGAAACGTTACTCAAGACTGGAT  
TATTTGATCAATGGGATCTATGTGGACATCTAAGGATGGAACCTCGGTGTCTCTTAATTCATT  
TAGTAACCAGAAGCCCAAATGCAATGAGTTTCTGCTGACTTGCTAGTCTTAGCAGGAGGTTG  
TATTTTGAAGACAGGAAAATGCCCCCTTCTGCTTTTCTCTTTTTTTTTTTTGGAGACAGAGTCTT  
GCTCTGTTGCCAGGCTGGAGTGAGTAGCACGATCTCGGCTCTCACCAGCAACCTCCGTCTC  
CTGGGTTCAAGCGATTCTCCTGCCTCAGCCTCCTAAGTATCTGGGATTACAGGCATGTGCCA  
CCACACCTGGGTGATTTTTGTATTTTTAGTAGAGACGGGGTTTTACCAGTGTGGTCAGGCTG  
GTCTCAAACCTCCTGACCTAGTGATCCACCCTCCTCGGCCTCCCAAAGTGCTGGGATTACAGG  
CATGAGCCACCACAGCTGGCCCCCTTCTGTTTTATGTTTGGTTTTTTGAGAAGGAATGAAGTG  
GGAACCAATTAGGTAATTTTGGGTAATCTGTCTCTAAAATATTAGCTAAAAACAAAGCTCT  
ATGTAAAGTAATAAAGTATAATTGCCATATAAATTTCAAATTTCAACTGGCTTTTATGCAAA  
GAAACAGGTTAGGACATCTAGGTTCCAATTCATTCACATTCTTGGTTCCAGATAAAATCAAC  
TGTTTATATCAATTTCTAATGGATTTGCTTTTCTTTTATATGGATTCCTTTAAACTTATT  
CCAGATGTAGTTCCTTCCAATTAAATATTTGAATAAATCTTTGTTACTCAA

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**FIGURE 328**

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45410
><subunit 1 of 1, 431 aa, 1 stop
><MW: 46810, pI: 6.45, NX(S/T): 6
MFFGGEGSLTYTLVIICFLTLRLSASQNCCLKSLEDVVIDIQSSLKGI RGNP VYTSTQED
CINSCCSTKNISGDKACNLMIFDTRKTARQPNCYLFFCPNEEACPLKPAKGLMSYRIITDFP
SLTRNLPSQELPQEDSLLHGQFSQAVTPLAHHHTDYSKPTDISWRDTLSQKFGSSDHLEKLF
KMDEASAQLLAYKEKGHSQSSQFSSDQEIAHLLPENVSALPATVAVASPH TTSATPKPATLL
PTNASVTPSGTSQPQLATTAPPVTTVTSQPPTTLISTVFTRAAATLQAMATTAVLTTTFQAP
TDSKGSLETIPFTEISNLT LNTGNVYNPTALSMSNVESSTMNK TASWEGREASPGSSSQGSV
PENQYGLPFEKWLLIGSLLFGVLFLVIGLVLLGRILSESLRRKRY SRLDYLINGIYVDI
```

**Signal sequence.**

amino acids 1-25

**Transmembrane domain.**

amino acids 384-405

**N-glycosylation sites.**

amino acids 72-76, 222-226, 251-255, 327-331, 352-356

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 415-419

**Tyrosine kinase phosphorylation site.**

amino acids 50-57

**N-myristoylation sites.**

amino acids 4-10, 48-54, 315-321

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**FIGURE 329**

CTCCACGGTGTCCAGCGCCCAGAAATGCGGCTTCTGGTCCTGCTATGGGGTTGCCTGCTGCT  
CCCAGGTTATGAAGCCCTGGAGGGCCCAGAGGAAATCAGCGGGTTCAAGGGGACACTGTGT  
CCCTGCAGTGCACCTACAGGGAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGT  
GGGATCCTCTTCTCTCGCTGCTCTGGCACCATCTATGCAGAAGAAGAAGGCCAGGAGACAAT  
GAAGGGCAGGGTGTCCATCCGTGACAGCCGCCAGGAGCTCTCGCTCATTGTGACCCTGTGGA  
ACCTCACCTGCAAGACGCTGGGGAGTACTGGTGTGGGGTCGAAAAACGGGGCCCCGATGAG  
TCTTTACTGATCTCTCTGTTTCGTCTTTCCAGGACCCTGCTGTCCTCCCTCCCCTTCTCCCAC  
CTTCCAGCCTCTGGCTACAACACGCCTGCAGCCCCAAGGCAAAAGCTCAGCAAACCCAGCCCC  
CAGGATTGACTTCTCCTGGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGG  
GCTGAGGGCCCCCTCATTGCCAGGGACTTCCCAGTACGGGCACGAAAGGACTTCTCAGTACAC  
AGGAACCTCTCCTCACCCAGCGACCTCTCCTCCTGCAGGGAGCTCCCGCCCCCCCATGCAGC  
TGGACTCCACCTCAGCAGAGGACACCAGTCCAGCTCTCAGCAGTGGCAGCTCTAAGCCCAGG  
GTGTCCATCCCGATGGTCCGCATACTGGCCCCAGTCCTGGTGCTGCTGAGCCTTCTGTCAGC  
CGCAGGCCTGATCGCCTTCTGCAGCCACCTGCTCCTGTGGAGAAAGGAAGCTCAACAGGCCA  
CGGAGACACAGAGGAACGAGAAGTTCTGGCTCTCACGCTTGACTGCGGAGGAAAAGGAAGCC  
CCTTCCCAGGCCCCCTGAGGGGGACGTGATCTCGATGCCTCCCCCTCCACACATCTGAGGAGGA  
GCTGGGCTTCTCGAAGTTTGTCTCAGCGTAGGGCAGGAGGCCCTCCTGGCCAGGCCAGCAGT  
GAAGCAGTATGGCTGGCTGGATCAGCACCGATTCCCGAAAGCTTTCCACCTCAGCCTCAGAG  
TCCAGCTGCCCCGACTCCAGGGCTCTCCCCACCCTCCCCAGGCTCTCCTCTTGTCATGTTCCA  
GCCTGACCTAGAAGCGTTTGTCTAGCCCTGGAGCCCAGAGCGGTGGCCTTGCTCTTCCGGCTG  
GAGACTGGGACATCCCTGATAGGTTACATCCCTGGGCAGAGTACCAGGCTGCTGACCCTCA  
GCAGGGCCAGACAAGGCTCAGTGGATCTGGTCTGAGTTTCAATCTGCCAGGAACCTCTGGGC  
CTCATGCCCAGTGTCTGGACCCTGCCTTCCCTCCCACTCCAGACCCCACCTTGTCTTCCCTCCC  
TGGCGTCTCAGACTTAGTCCCACGGTCTCCTGCATCAGCTGGTGATGAAGAGGAGCATGCT  
GGGGTGAGACTGGGATTCTGGCTTCTCTTTGAACCACCTGCATCCAGCCCTTCAGGAAGCCT  
GTGAAAAACGTGATTCTCTGGCCCCACCAAGACCCACCAAAACCATCTCTGGGCTTGGTGCAG  
GACTCTGAATTCTAACAAATGCCCAGTGACTGTCTGCACTTGAGTTTGAGGGCCAGTGGGCCTG  
ATGAACGCTCACACCCCTCAGCTTAGAGTCTGCACTTGGGCTGTGACGTCTCCACCTCCCC  
CAATAGATCTGCTCTGTCTGCGACACAGATCCACGTGGGGACTCCCTGAGGCCTGCTAAG  
TCCAGGCCTTGGTCAGGTGAGGTGCACATTGCAGGATAAGCCCAGGACCGGCACAGAAGTGG  
TTGCCTTTNCCATTTGCCCTCCCTGGNCCATGCCTTCTTGCTTTGGAAAAAATGATGAAGA  
AAACCTTGGCTCCTTCTTGTCTGGAAAGGGTTACTTGCCTATGGGTTCTGGTGGCTAGAGA  
GAAAAGTAGAAAACCAGAGTGCACGTAGGTGTCTAACACAGAGGAGTAGGAACAGGGCGG  
ATACCTGAAGGTGACTCCGAGTCCAGCCCCCTGGAGAAGGGGTGCGGGGTGGTGGTAAAGTA  
GCACAATACTATTTTTTTTCTTTTTCCATTATTATTGTTTTTTAAGACAGAATCTCGTGCT  
GCTGCCCAGGCTGGAGTGCAGTGGCACGATCTGCAAACTCCGCCTCCTGGGTTCAGTGATT  
CTTCTGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGCACGCACCACCACACCTGGCTAATT  
TTTGTACTTTTAGTAGAGATGGGGTTTCACCATGTTGGCCAGGCTGGTCTTGAACCTCTGAC  
CTCAAATGAGCCTCCTGCTTCAGTCTCCCAAATTGCCGGGATTACAGGCATGAGCCACTGTG  
TCTGGCCCTATTTCTTTAAAAAGTGAAATTAAGAGTTGTTAGTATGCAAACTTGGAAG  
ATGGAGGAGAAAAAGAAAAGGAAGAAAAAATGTCACCCATAGTCTCACCAGAGACTATCAT  
TATTTCTGTTTTGTTGTACTTCCCTCCACTCTTTTCTTCTTACATAATTTGCCGGTGTCTT  
TTTACAGAGCAATTATCTTGTATATACAACCTTTGTATCCTGCCTTTTCCACCTTATCGTTCC  
ATCACTTTATTCCAGCACTTCTCTGTGTTTTACAGACCTTTTTATAAATAAAATGTTCA  
GCTGCATAAAAAAAAAAAAAA



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**FIGURE 330**

&lt;/usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44196

&lt;subunit 1 of 1, 332 aa, 1 stop

&lt;MW: 36143, pI: 5.89, NX(S/T): 1

MRLLVLLWGCLLLPGYEALEGP EEISGFEGDTVSLQCTYREELRDHRKYWCRKGGILFSRCS  
GTIYAEEEGQETMKGRVSIRDSRQELSLIVTLWNLTLQDAGEYWCGVEKRGPD E SLLISLFV  
FPGPCCPPSPSPPTFQPLATTRLQPKAKAQQTQPPGLTSPGLYPAATTAKQGKTGA EAPPLPG  
TSQYGHERTSQYTGTSPHPATSPAGSSRPPMQLDSTSAEDTSPALSSGSSKPRVSIPMVRI  
LAPVLVLLSLLSAAGLIAFCSHLLLWRKEAQQATETQRNEKFWLSRLTAE EKEAPSQAPEGD  
VISMPPLHTSEEELGFSKFVSA

**Important features:****Signal peptide:**

amino acids 1-17

**Transmembrane domain:**

amino acids 248-269

**N-glycosylation site.**

amino acids 96-99

**Fibrinogen beta and gamma chains C-terminal domain.**

amino acids 104-113

**Ig like V-type domain:**

amino acids 13-128

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08439

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/47 C07K14/705 C12N15/62 C07K16/18  
 G01N33/53 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

STRAND

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 39448 A (HUMAN GENOME SCIENCES INC) 11 September 1998 (1998-09-11) see passages relating to gene 174 (clone H2MBF44) and the claims. ---	1-28
X	WO 98 42741 A (GENETICS INST) 1 October 1998 (1998-10-01) see passages relating to clone ck181_7 and the claims. ---	1-28
A	EP 0 834 563 A (SMITHKLINE BEECHAM CORP) 8 April 1998 (1998-04-08) the whole document ---	
A	WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document ---	
	-/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## ° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

16 August 2000

Date of mailing of the international search report

13.11.00

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Authorized officer

Smalt, R

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator" GENE,NL,ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 163, no. 2, 3 October 1995 (1995-10-03), pages 193-196, XP004041983 ISSN: 0378-1119 the whole document ---	
A	KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA,US,NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document ---	
P,X, L	WO 99 63088 A (BAKER KEVIN ;CHEN JIAN (US); GENENTECH INC (US); YUAN JEAN (US); G) 9 December 1999 (1999-12-09) see passages relating to PR0281 and the claims. L: priority. ---	1-28
P,X	WO 99 46375 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 16 September 1999 (1999-09-16) see whole document, particularly passages relating to seq.ID'2 219 and 251 ---	1-13, 17-28
P,X	WO 99 53040 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 21 October 1999 (1999-10-21) page 1 -page 8 see claims. page 128 ---	1-13, 17-22, 24-28
P,X	WO 00 08145 A (NOVARTIS ERFINDUNGEN VERWALTUN ;NOVARTIS AG (CH); HOLNESS CLAIRE L) 17 February 2000 (2000-02-17) the whole document ---	1-13, 21-28
P,X	WO 99 63083 A (TSURITANI KATSUKI ;ARASE SEIJI (JP); IKEDA AKIKO (JP); TAISHO PHAR) 9 December 1999 (1999-12-09) abstract see sequences. -----	1-13,21, 22,25-28

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/08439

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-28, All partially.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-28, all partially

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0281 (seq.ID.2), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0281, chimeric protein comprising a portion corresponding to PR0281, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto.

2. Claims: Inventions 2-132: claims 1-28,  
all partially and claims 4 and 13 as far as  
applicable

Subject matter as defined for invention 1 above, but limited to the respective amino acid sequences and corresponding nucleic acid sequences referred to as:

2. PR0276 (seq.ID's 5/6),
3. PR0189 (Seq.ID's 7/8),
4. PR0190 (Seq.ID's 13/14),
5. PR0341 (Seq.ID's 19/20),
6. PR0180 (Seq.ID's 22/23),
7. PR0190 (Seq.ID's 13/14),
8. PR0194 (Seq.ID's 27/28),
9. PR0203 (Seq.ID's 29/30),
10. PR0290 (Seq.ID's 32/33),
11. PR0874 (Seq.ID's 35/36),
12. PR0710 (Seq.ID's 40/41),
13. PR01151 (Seq.ID's 46/47),
14. PR01281 (Seq.ID's 51/52),
15. PR0358 (Seq.ID's 56/57),
16. PR01310 (Seq.ID's 61/62),
17. PR0698 (Seq.ID's 66/67),
18. PR0732 (Seq.ID's 72/73),
19. PR01120 (Seq.ID's 83/84),
20. PR0537 (Seq.ID's 94/95),
21. PR0536 (Seq.ID's 96/97),
22. PR0535 (Seq.ID's 98/99),
23. PR0718 (Seq.ID's 102/103),
24. PR0872 (Seq.ID's 112/113),
25. PR01063 (Seq.ID's 114/115),
26. PR0619 (Seq.ID's 116/117),
27. PR01188 (Seq.ID's 123/124),
28. PR0784 (Seq.ID's 134/135),
29. PR0783 (Seq.ID's 137/138),
30. PR0820 (Seq.ID's 145/146),

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

31. PRO1080 (Seq.ID's 147/148),
32. PRO1079 (Seq.ID's 150/151),
33. PRO793 (Seq.ID's 152/153),
34. PRO1016 (Seq.ID's 155/156),
35. PRO1013 (Seq.ID's 157/158),
36. PRO937 (Seq.ID's 159/160),
37. PRO842 (Seq.ID's 164/165),
38. PRO839 (Seq.ID's 166/167),
39. PRO1180 (Seq.ID's 168/169),
40. PRO1134 (Seq.ID's 170/171),
41. PRO830 (Seq.ID's 174/175),
42. PRO1115 (Seq.ID's 176/177),
43. PRO1277 (Seq.ID's 178/179),
44. PRO1135 (Seq.ID's 180/181),
45. PRO828 (Seq.ID's 188/189),
46. PRO1009 (Seq.ID's 193/194),
47. PRO1007 (Seq.ID's 196/197),
48. PRO1056 (Seq.ID's 198/199),
49. PRO826 (Seq.ID's 200/201),
50. PRO819 (Seq.ID's 202/203),
51. PRO1006 (Seq.ID's 204/205),
52. PRO1112 (Seq.ID's 206/207),
53. PRO1074 (Seq.ID's 208/209),
54. PRO1005 (Seq.ID's 210/211),
55. PRO1073 (Seq.ID's 212/213),
56. PRO1152 (Seq.ID's 215/216),
57. PRO1136 (Seq.ID's 218/219),
58. PRO813 (Seq.ID's 220/221),
59. PRO809 (Seq.ID's 222/223),
60. PRO791 (Seq.ID's 224/225),
61. PRO1004 (Seq.ID's 226/227),
62. PRO1111 (Seq.ID's 228/229),
63. PRO1344 (Seq.ID's 230/231),
64. PRO1109 (Seq.ID's 235/236),
65. PRO1383 (Seq.ID's 240/241),
66. PRO1003 (Seq.ID's 245/246),
67. PRO1108 (Seq.ID's 247/248),
68. PRO1137 (Seq.ID's 249/250),
69. PRO1138 (Seq.ID's 252/253),
70. PRO1054 (Seq.ID's 255/256),
71. PRO994 (Seq.ID's 257/258),

### 3. Claim : 1

72. PRO812 (Seq.ID's 259/260),
73. PRO1069 (Seq.ID's 261/262),
74. PRO1129 (Seq.ID's 263/264),
75. PRO1068 (Seq.ID's 265/266),
76. PRO1066 (Seq.ID's 267/268),
77. PRO1184 (Seq.ID's 269/270),
78. PRO1360 (Seq.ID's 271/272),
79. PRO1029 (Seq.ID's 273/274),
80. PRO1139 (Seq.ID's 275/276),
81. PRO1309 (Seq.ID's 277/278),

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

82. PR01028 (Seq.ID's 280/281),
83. PR01027 (Seq.ID's 282/283),
84. PR01107 (Seq.ID's 284/285),
85. PR01140 (Seq.ID's 286/287),
86. PR01106 (Seq.ID's 288/289),
87. PR01291 (Seq.ID's 290/291),
88. PR01105 (Seq.ID's 292/293),
89. PR0511 (Seq.ID's 294/295),
90. PR01104 (Seq.ID's 296/297),
91. PR01100 (Seq.ID's 298/299),
92. PR0836 (Seq.ID's 300/301),
93. PR01141 (Seq.ID's 302/303),
94. PR01132 (Seq.ID's 308/309),
95. PR01346 (Seq.ID's 313/314),
96. PR01131 (Seq.ID's 318/319),
97. PR01281 (Seq.ID's 325/326),
98. PR01064 (Seq.ID's 333/334),
99. PR01379 (Seq.ID's 339/340),
100. PR0844 (Seq.ID's 344/345),
101. PR0848 (Seq.ID's 346/347),
102. PR01097 (Seq.ID's 348/349),
103. PR01153 (Seq.ID's 350/351),
104. PR01154 (Seq.ID's 352/353),
105. PR01182 (Seq.ID's 356/357),
106. PR01155 (Seq.ID's 358/359),
107. PR01156 (Seq.ID's 360/361),
108. PR01098 (Seq.ID's 362/363),
109. PR01127 (Seq.ID's 364/365),
110. PR01126 (Seq.ID's 366/367),
111. PR01125 (Seq.ID's 368/369),
112. PR01186 (Seq.ID's 370/371),
113. PR01198 (Seq.ID's 372/373),
114. PR01158 (Seq.ID's 374/375),
115. PR01159 (Seq.ID's 376/377),
116. PR01124 (Seq.ID's 378/379),
117. PR01287 (Seq.ID's 380/381),
118. PR01312 (Seq.ID's 386/387),
119. PR01192 (Seq.ID's 388/389),
120. PR01160 (Seq.ID's 393/394),
121. PR01187 (Seq.ID's 398/399),
122. PR01185 (Seq.ID's 400/401),
123. PR01345 (Seq.ID's 402/403),
124. PR01245 (Seq.ID's 407/408),
125. PR01358 (Seq.ID's 409/410),
126. PR01195 (Seq.ID's 411/412),
127. PR01270 (Seq.ID's 413/414),
128. PR01271 (Seq.ID's 415/416),
129. PR01375 (Seq.ID's 417/418),
130. PR01385 (Seq.ID's 419/420),
131. PR01384 (Seq.ID's 423/424),
132. PR09828 (Seq.ID's 510/511).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

4. Claims: Invention 133: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0943 (seq.ID.118), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0943, chimeric protein comprising a portion corresponding to PR0943, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa.

5. Claims: Inventions 134-136: claims 1-36,69-74,99-102,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0183 (seq.ID.495), PR0184 (seq.ID.497) or PR0185 (seq.ID.499), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa, whereby invention 134 is limited to PR0183, invention 135 is limited to PR0184, and invention 136 is limited to PR0185.

6. Claims: Invention 137: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable



## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0331 (seq.ID.501), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0331, chimeric protein comprising a portion corresponding to PR0331, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

7. Claims: Invention 138: claims 1-28,37-44,75-80,103-106,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01133 (seq.ID.129), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protien, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR01133 through interaction with PR0331 and vice versa, method of linking a bioactive molecule to a cell expressing PR0331 using PR01133 as binding ligands and vice versa, and method of modulating the activity of PR0331 by binding with PR01133, and vice versa.

8. Claims: Invention 139: claims 1-28,45-52,81-86,107-110,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01387 (seq.ID.422), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01387, chimeric protein comprising a portion corresponding to PR01387, antibody against said protein, the isolated extracellular domain of said protein or a protein with at

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa.

9. Claims: Invention 140 and 141: claims 1-28,45-52,81-86, 107-110,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0363 (seq.ID.503) or PR05723 (seq.ID.505), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0363 or PR05723 through interaction with PR01387 and vice versa, method of linking a bioactive molecule to a cell expressing PR01387 using PR0363 or PR05723 as binding ligands and vice versa, and method of modulating the activity of PR01387 by binding with PR0363 or PR05723, and vice versa, whereby invention 140 is limited to PR0363 and invention 141 is limited to PR05723.

10. Claims: Invention 142: claims 1-28, 53-60,87-92,111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01114 (seq.ID.183), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01114, chimeric protein comprising a portion corresponding to PR01114, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa,

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa.

11. Claims: Invention 143 and 144: claims 1-28, 53-60, 87-92, 111-114,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR03301 (seq.ID.507) or PR09940 (seq.ID.509), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR03301 or PR09940 through interaction with PR01114 and vice versa, method of linking a bioactive molecule to a cell expressing PR01114 using PR03301 or PR09940 as binding ligands and vice versa, and method of modulating the activity of PR01114 by binding with PR03301 or PR09940, and vice versa, whereby invention 143 is limited to PR03301 and invention 144 is limited to PR09940.

12. Claims: Invention 145: claims 1-28, 61-69, 93-98, 115-118,  
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR01181 (seq.ID.355), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR01181, chimeric protein comprising a portion corresponding to PR01181, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR07170, PR0361 or PR0846 through interaction with PR01181 and vice versa, method of linking a bioactive molecule to a cell expressing PR01181 using PR07170, PR0361 or PR0846 as binding ligands and vice versa, and method of modulating the activity of PR01181 by binding with PR07170, PR0361 or PR0846, and vice versa.

13. Claims: Inventions 146-148: claims 1-28, 61-69, 93-98,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

115-118,  
all partially and claims 4 and 13 as far as  
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO7170 (seq.ID.513), PRO361 (seq.ID.515) or PRO846 (seq.ID.517), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO7170, PRO361 or PRO846 through interaction with PRO1181 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1181 using PRO7170, PRO361 or PRO846 as binding ligands and vice versa, and method of modulating the activity of PRO1181 by binding with PRO7170, PRO361 or PRO846, and vice versa, whereby invention 146 is limited to PRO7170, invention 147 is limited to PRO361, and invention 148 is limited to PRO846.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/08439

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9839448	A	11-09-1998	AU 6545398 A EP 0972029 A EP 0972030 A WO 9839446 A	22-09-1998 19-01-2000 19-01-2000 11-09-1998
WO 9842741	A	01-10-1998	AU 6777298 A EP 0998490 A	20-10-1998 10-05-2000
EP 0834563	A	08-04-1998	JP 10179178 A US 5824504 A	07-07-1998 20-10-1998
WO 9707198	A	27-02-1997	US 5707829 A AU 6712396 A AU 6768596 A CA 2227220 A CA 2229208 A EP 0839196 A EP 0851875 A JP 11510045 T US 6043344 A WO 9704097 A US 6074849 A US 5969093 A	13-01-1998 18-02-1997 12-03-1997 06-02-1997 27-02-1997 06-05-1998 08-07-1998 07-09-1999 28-03-2000 06-02-1997 13-06-2000 19-10-1999
WO 9963088	A	09-12-1999	AU 4328699 A AU 2212299 A WO 9935170 A	20-12-1999 26-07-1999 15-07-1999
WO 9946375	A	16-09-1999	DE 19811194 A	16-09-1999
WO 9953040	A	21-10-1999	DE 19817557 A	21-10-1999
WO 0008145	A	17-02-2000	AU 5730099 A	28-02-2000
WO 9963083	A	09-12-1999	JP 11332571 A AU 3955099 A	07-12-1999 20-12-1999